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PRECANCEROUS DERMATOSES*

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PRECANCEROUS dermatoses as discussed in this paper include a group of lesions that are not malignant but in or on which cancer may develop.

The most important precancerous conditions are the keratoses. This group includes senile, arsenical, tar, paraffin and roentgen-ray keratoses and leukoplakia. The precancerous dermatosis of Bowen is probably a distinct type of epithelioma, although much confusion exists as to its limitations. Erythroplasia of Queyrat is a classic precancerous disease.

Carcinoma is a prominent feature in xeroderma pigmentosum, and malignant growths frequently develop in or from pigmented moles. In sailors, farmers, mountaineers and other persons much exposed to the sun's rays and all weather conditions, a presenile dystrophy characterized by atrophy, pigmentation, telangiectasis and keratosis occurs and not infrequently terminates in multiple epithelioma. Whether or not Paget's disease is cancerous in the stage of dermatitis is still a debated question, but there is no doubt that it should be so viewed and treated. The association of kraurosis vulvae and carcinoma is well known, and malignant transformation is of great importance in this disease.

Epitheliomas develop occasionally in keratosis follicularis (Darier's disease), lupus vulgaris, lupus erythematosus, psoriasis and scleroderma, in old scars, particularly those following burns, on cutaneous horns and callosities and in wens, dermoid cysts, ulcers and fistulas.

Montgomery[1] would limit the term "precancerous dermatosis" to Bowen's precancerous dermatosis, senile keratosis, arsenical keratosis, tar and radiation keratosis, leukoplakia and the erythroplasia of Queyrat. He states that in 20 per cent or more of these cases epitheliomas of squamous type develop.

HYPERKERATOSES

Senile Keratosis

The most significant form of keratosis terminating in cancer and the one to which the term "precancerous" is appropriate is the senile keratoma of Besnier. In a paper presented at the International Congress of 1896 in London, Dubreuilh[2] gave a clear description of circumscribed keratosis and adopted Besnier's title, which Eller and Ryan[3] consider a misnomer — they prefer the term "senile keratosis."

These lesions are seen in people past middle life, oftener in men than in women, and occur on surfaces exposed to the sun and changing weather conditions. The common regions affected are the forehead, the temple, the upper part of the cheeks, the nose, the dorsal surfaces of the hands, the sides of the neck and the ears. The growths are occasionally seen elsewhere. They are pinhead to dime-sized, moderately elevated, sometimes slightly greasy but more frequently dry and hard, firmly adherent, yellowish-brown or black crusts; when forcibly removed, they present on the undersurface numerous horny spines, which have projected into the dilated mouths of the underlying follicles. The skin beneath is uneven, moist and red, bleeds readily and is sometimes superficially ulcerated. The lesions commonly present no inflammatory symptoms, but while they are changing into true epitheliomas some inflammatory reaction may be noted. The course is variable. The process may remain for years without change. Some growths are gradually transformed into epitheliomatous ulcers that gradually enlarge, whereas others become more elevated and wartlike and present the clinical characteristics of a papillomatous epithelioma.

These lesions are often found in association with other changes characteristic of the senile skin, such as atrophy, hyperpigmentations and unusual

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dryness, with or without scaling and with more or less persistent seborrheic patches.

The histopathology of senile keratosis was studied early by Hartzell[4] and Fordyce[5] and later restudied, together with verruca senilis (verruca seborrheica), by Freudenthal,[6] Eller and Ryan,[3] Hookey[7] and Montgomery and Dörffel.[8] This condition presents a marked hyperkeratosis, which consists of closely packed horny lamellae, and an irregular acanthosis, the basal layer being poorly defined and its cells containing a variable amount of pigment. There are a variable number of mitoses in the epidermal cells, and dyskeratotic phenomena are seen. In the upper cutis there occurs an inflammatory reaction of varying degree of intensity, indicated by vascular dilatation, and a cellular infiltration consisting chiefly of lymphocytes, together with a few plasma and connective-tissue cells. Some basophilic degeneration of the cutis also occurs.

The senile flat wart, verruca seborrheica, often closely resembles the senile keratoma. The lesions of verruca seborrheica occur usually at or past middle life and are found chiefly on the back, over the shoulders, on the chest, on the abdomen at the waistline and occasionally on the face and neck. They are flat, moderately elevated, oval or round, pea to small-coin sized, gray, yellow, brown or black, and present a soft granular surface. The friable greasy crust is easily removed, revealing a red granular or slightly papillomatous base. The lesions may be accompanied by itching, which at times may be severe. Unlike the senile keratoses, they rarely undergo malignant transformation. Occasionally, the surface is smooth, when the process resembles a nonhairy pigmented mole; this type has been designated "nevoid keratosis."

In addition to the typical verruca seborrheica described above, there occurs a hyperkeratotic seborrheic keratosis in the form of scaling pigmented patches that closely resemble senile keratoses. In these the scales are waxy and the skin is thickened, sometimes slightly verrucous; their color is yellow brown to brownish black, and they are found on the face, scalp and upper portion of the trunk in elderly people. These not infrequently undergo malignant transformation.

The characteristic changes consist in hyperkeratosis, acanthosis, horny cysts and hyperpigmentation. The epithelial hyperplasia occurs in the form of a loose or solid network of epithelial cells. Islands of connective tissue are enclosed in this network, owing to the irregular acanthotic prolongation of the rete. Numerous horny cysts are present and are characteristic of the affection. Hyperpigmentation occurs, the melanin granules being scattered throughout the epidermis as well as being present in the basal layer of epithelial cells; they are also found in the cutis. No dyskeratotic changes are found in the epithelial cells. The cutis may show a moderate inflammatory reaction.

Hookey[7] summarizes the changes as follows: senile keratoses are characterized by hyperkeratosis and irregular acanthosis, with dyskeratotic phenomena and secondary inflammatory reaction; seborrheic keratoses are distinguished by hyperkeratosis and irregular acanthosis with the formation of an epithelial network, absence of dyskeratosis, a mild inflammatory reaction and, usually, increased pigmentation. The chief points of distinction clinically between the two conditions are their location and appearance. Senile keratoses occur mainly on the forehead, the upper portions of the sides of the face, the ears, the sides of the neck and the dorsums of the hands. The lesions are hard, firmly adherent crusts, with horny spines on the undersurface, which fit into the open mouths of follicles beneath. The surface beneath the crust is moist and red, bleeds easily and is sometimes superficially ulcerated. The seborrheic keratoses are found on the trunk, front and back, the abdomen and, less often, the face and neck. These lesions are soft and granular and easily removed, revealing a soft granular or slightly papillomatous base. The senile keratoses often undergo malignant transformation and are therefore precancerous, whereas the seborrheic keratoses rarely undergo this change and are not considered precancerous.

The lesions of keratosis senilis may be removed by softening with a keratolytic (salicylic acid) ointment for a few days, then curetting the surface and refrigerating with carbon dioxide snow, or trichloracetic acid may be employed. Diathermy and electrocoagulation are also used. If malignant change is already present, one or the other of the last two methods or surgical excision is preferable.

As a rule, the removal of seborrheic keratoses or warts is necessary only for cosmetic purposes. When they are numerous and large and limited to the trunk, complete removal is not necessary. They may be reduced in size and made less conspicuous by the use of an ointment containing 3 per cent salicylic acid and 5 per cent sulfur. If complete removal is desired, they may be curetted and frozen with carbon dioxide snow, or trichloracetic acid may be applied. Roentgen-ray therapy is also efficacious.

Keratoses occur quite commonly on the lips, especially the lower. They are often small or oval lesions, moderately elevated. At times they are

linear and may cover half the surface of the lip in the form of a narrow band. They usually occur in men around middle life and older, although they are not infrequently seen at an earlier age. They are persistent and often undergo malignant ulceration. They should always be viewed as having dangerous potentialities, and they should be thoroughly removed as early as possible.

Leukoplakia

Leukoplakia, as seen in the mouth, occurs as whitened areas of varying size and diverse outline. There may be one or several patches on the surface of the tongue, beneath the tongue, on the buccal mucosa, particularly behind the commissures and over the area opposite the molars, on the gums, on the lips and on the hard palate. At times the lesions occur profusely over a large portion of the buccal cavity. The patches are white or grayish white, thickened in varying degrees, often rough. Erosions occur in patches when the superficial covering is shed. At times the patch becomes verrucous, fissured and vegetating. It is not known in what proportion cancer develops. The process occurs in both syphilitic and nonsyphilitic persons. The chief lesion from which it is to be distinguished is lichen planus, in which the white areas are linear and striate on the buccal mucosa and consist of white papules on the tongue. The presence of cutaneous lesions of lichen planus is a valuable diagnostic point. Occasionally a syphilitic interstitial glossitis with atrophy is associated with leukoplakia. The use of tobacco, both by smoking and chewing, is often an etiologic factor.

In treatment, cessation of the use of local irritants is primarily indicated, the first one being tobacco. Hot and cold food, condiments and vinegar are to be avoided. Electrodesiccation, the electric cautery and radium are the most efficient methods of direct removal. In extensive quiescent cases, palliative treatment is recommended. Partial removal is likely to induce malignant change.

Kraurosis vulvae usually occurs in women of advanced age or at the menopause, or in younger women in whom the condition has been produced by surgical removal of the uterus or ovaries. It is essentially a sclerosing atrophy of the mucocutaneous structures of the vulva. In advanced cases it is characterized by the complete, or almost complete, disappearance of the labia minora, the frenulum and the clitoris, with flattening and reduction in the volume of the labia majora; rigidity of all the vulvar tissues and atresia of the vaginal orifice are also noticeable The retracted tissues may be whitish, yellowish, reddish or bluish. A characteristic glistening or varnished appearance may be present. The lesion is usually preceded by intense itching, which may persist, although in some late cases there is a loss of cutaneous sensibility. Taussig[9] states that 75 per cent occur at the menopause, and that the remainder have some disturbance of ovarian function. True leukoplakia may occur as a complication; if so, cancer often follows.

This condition is to be distinguished from simple leukoplakia of this region, which is similar to that seen in the mouth, and from pruritus with lichenification (neurodermatitis), which produces a whitish thickening of the vulva. When the last condition is present, the usual picture of neurodermatitis is apt to extend over the pubes and down over the inner aspects of the thighs.

The treatment of kraurosis, with or without leukoplakia, is surgical. Taussig[9] believes that the incidence of cancer can be reduced 50 per cent by complete vulvectomy for leukoplakic vulvitis.

Montgomery and associates[10] give the following characteristic histologic features of leukoplakia: hyperkeratosis; hypertrophy of the stratum granulosum; atrophy of the rete mucosum; liquefaction necrosis of the basal-cell layer; edema and homogenization of the connective-tissue fibers; cellular infiltration, largely lymphocytic, of the mid-cutis; and subsequent atrophy of the cutis and subcutis.

Precancerous Dermatosis of Bowen

In 1912 Bowen[11] recorded two cases of chronic atypical epithelial proliferation with unique clinical characteristics. Since that time, numerous cases have been recorded, a number of which have differed materially from the original cases reported. As the term denotes, Bowen believed that malignant transformation was probable, and in a number of cases since recorded such transformation has occurred.

In Bowen's cases there were lesions in well-defined patches. The early lesion was a firm pale-red papule covered with a thickened horny layer or a cornified crust. Beneath the crust the surface was papillomatous. Enlargement of the papule formed lenticular or rounded nodular lesions that were discrete or grouped and confluent. The lesions at the margins of the patch had an annular or serpiginous outline. The patches increased in size by the formation of new lesions at the periphery. The clinical appearance suggested a late nodular syphiloderm.

The chief histopathologic changes occur in the epidermis. There is a marked proliferation of the rete, with distortion of its cells. There is amitotic cell division, with clumping of the nuclei, and individual cell keratinization, with the forma-

tion of giant epithelial cells. Vacuolization of the cells occurs, simulating the cell of Paget's disease. The intercellular bridges are preserved, and the basal layer is intact. In the upper corium there is a vascular dilation with a cellular infiltration consisting of lymphocytic and plasma cells.

The process is to be distinguished from extramammary Paget's disease and superficial epitheliomatosis. The localization of the lesions described by Bowen, with their papular and nodular character and serpiginous configuration, makes the clinical distinction from the superficial red scaling or crusted patches seen in Paget's disease.

In all cases, surgical removal is recommended.

Pigmented Moles

The most dangerous type of mole is flat and slaty or blue black. These moles are commonly seen near the eyes and on the feet. They sometimes undergo malignant transformation without apparent injury. As a rule, however, chronic irritation, trauma, application of caustics or incomplete surgical removal is the immediate cause of malignant change. The moles that are large, brown, flat or elevated, and hairy or free from hair are not usually a menace unless irritated. I have seen quite a large number of generalized fatal cases of malignant melanoma that have followed incomplete surgical removal or cauterization (usually with an acid) of a pigmented mole. As a rule the malignant metastatic tumors are classed as nevocarcinoma or malignant melanoma. Nomland[12] described multiple basal-cell, pigmented epitheliomas developing on basal-cell pigmented nevi.

Erythroplasia of Queyrat

This is a rare lesion, originally described by Fournier and Darier[13] as a precancerous condition. It occurs on the glans, the prepuce and the vulva, as well as on the buccal mucosa, including the tongue, cheeks and lips. The lesions are well-defined areas with brilliant-red velvety surfaces. The condition progresses slowly and indefinitely, and it is resistant to local treatment. The cause is unknown, although the process is often associated with syphilis. Conditions from which it must be distinguished are superficial epithelioma, tuberculosis and syphilis.

The characteristic histologic change consists in marked acanthosis, with some cellular infiltration in the upper cutis. Occasionally, dyskeratotic changes, such as those seen in Bowen's disease, occur. Carcinoma always follows, unless the growth is totally destroyed in its early stages.

Keratosis Follicularis

Keratosis follicularis (Darier's disease) is a classic keratotic disease, first described by Morrow[14] and shortly thereafter independently studied by Darier,[15] of France, and White,[16] of America. It was early studied intensively on account of peculiar round bodies, found on microscopic examination, which were believed to be parasites (psorosperms). In his histologic examination of White's original case, Bowen[17] described these bodies as epithelial cells that had undergone anomalous cornification. The disease occurs at all ages, not infrequently beginning in infancy, and is also seen in elderly people. Males are attacked more frequently than females, and heredity is a factor in its production. Trimble,[18] for example, recorded 5 cases in three generations.

The disease is characterized by an eruption beginning as papules, which soon become crust covered and by coalescence produce papillomatous vegetating and tumorlike growths. The eruption is usually most extensive on the trunk, especially in the axillary and inguinal regions and around the neck. It also occurs on the head and extremities. The vegetating and papillomatous lesions are found chiefly in the axillary and genital regions and behind the ears. Seborrheic crusting occurs in the scalp. The early lesion is essentially a follicular keratosis.

The essential pathologic process is a hyperkeratosis of the follicles, which are filled with horny material. The round bodies are found between the prickle cells of the rete malpighii. The disease is uncommon, although numerous examples have been seen all over the world. Wende[19] recorded the first example of malignant transformation seen in this affection.

Treatment is unsatisfactory. Amelioration of the symptoms may be effected with the use of keratolytic ointments and roentgen-ray therapy. The prognosis as to recovery from the disorder is unfavorable, but as to a serious termination it is good, aside from the possibility of malignant transformation.

Paget's Disease

This disease, as seen on the nipple, was first described by Paget[20] in 1874. Extramammary cases were reported many years later (Hartzell[21]).

The nipple cases usually occur on the breasts of women, although some have occurred in men. On the nipple the process is characterized by redness and scaling, which later becomes more marked; the redness deepens, and the surface becomes granulating and exudes a clear viscid secretion forming

crusts, accompanied by sensations of heat, burning and itching of varying intensity. The inflammatory area is well defined, and as time progresses the process extends deeply, forming a circumscribed infiltration of the skin that on palpation suggests a large-sized coin or button in the substance of the areola and surrounding parts. The nipple becomes flattened or retracted. Sooner or later carcinomatous infiltration occurs in the substance of the breast. The course of the disease is usually slow, and no attempt at healing of the eczematous process on the nipple occurs.

Extramammary cases have been seen on the penis, scrotum, buttocks, vulva and perineum and in the axilla and numerous other situations. The clinical symptoms are those seen on the nipple. It is likely that the major portion of the lesions on the trunk are examples of superficial epitheliomatosis, which is usually of the basal-cell type.

The characteristic histologic changes consist in edema and hypertrophy of the epidermis, in which peculiar cells are found, together with an inflammatory cellular infiltration in the corium. There is marked hypertrophy of the rete with downward growth of its pegs into the corium. Peculiar double-contoured cells of large size are found in varying numbers. These cells are vacuolated, round or irregular, and often contain two or three nuclei that show varying changes in form, size and location. The Paget cells resemble the dyskeratotic cells found in Bowen's disease, but they have no intercellular bridges. They were formerly considered by Darier to be coccidia or psorosperms, but it is now known that they are cellular degenerations.

A cellular infiltration, consisting of leukocytes, small connective tissue, plasma and a few mast cells, is found in the corium, together with dilatation of the blood vessels, and in the areas of infiltration the collagen and elastin are more or less destroyed. The retraction of the nipple is due to sclerosis occurring around the mammary ducts, the latter being involved in malignant infiltration early in the process in some cases. The subsequent carcinoma may develop either from these ducts or glands beneath or from the surface epithelium.

The histology of the extramammary cases corresponds to the above in most particulars. In some cases the cellular exudate is less pronounced. The presence of the Paget cell and other characteristics identify the condition histologically. Montgomery[22] believes that most of the cases reported as extramammary Paget's disease, particularly those on the scrotum, perineum and penis, were histologically frank squamous-cell epitheliomas showing individual cell keratinization, whereas those on other parts of the body histologically were basal-cell epitheliomas, the lesions of Bowen's disease or metastatic carcinomas.

Paget's disease of the breast is distinguished from eczema by its intractable character, its localization to the nipple area, its deeper infiltration — shown clinically by a feeling of hardness revealed by palpation — and, finally, its accompanying malignant growth in the substance of the breast. The reported extramammary cases on the trunk are practically indistinguishable from superficial epitheliomatosis in its crusted type.

Paget's disease of the breast requires surgical extirpation. Complete removal of the breast and accompanying lymph nodes is recommended. The extramammary type may be excised or treated with radium or roentgen rays.

Xeroderma Pigmentosum

Xeroderma pigmentosum is a rare disease that begins in childhood and is characterized by hyperpigmentation, atrophic areas, telangiectases and warty and malignant growths. This disease was first described by Hebra and Kaposi[23] in 1870.

The eruption occurs largely on exposed surfaces, including the face, neck, upper chest, hands and forearms. Other areas are occasionally invaded. Sunburn has initiated the process in several cases. It is distinctly a family disease, being present in two or more members as a rule. The earliest symptom may be an erythema or dermatitis. Following this, or independent of it, frecklelike lesions develop. These become numerous, are of variable sizes and present different shades of yellow and brown. Interspersed between these lesions, variously sized whitish atrophic areas or cicatriform patches develop. Telangiectases and small angiomas are common. Flat or convex warty growths also develop, and these resemble senile keratoses. They are pea sized or larger and are scattered among the pigmented and telangiectatic lesions. At a later date malignant growths appear, and various forms occur, the chief of which is carcinoma. Ectropion is common, with its associated photophobia and lacrimation, and often causes ulceration on the face. Keratitis is common, and nodules and opacities occur in the cornea, causing obstruction of vision.

The progress of the disease is usually slow, though death from marasmus may occur within a few months. Malignant transformation usually occurs after many years and results in a fatal termination. A striking characteristic of the disease is its resemblance to the changes seen in the senile skin. Aside from the fact that it is a family affection and apparently is the result of the action

of the sun's rays on a peculiarly sensitive skin, nothing is known of its cause.

All the changes seen microscopically are closely simulated in sailors' skin and in chronic roentgen-ray dermatitis. The malignant growths oftenest seen are basal-cell epitheliomas. In addition, melanoepitheliomas, trichoepitheliomas, round-cell, spindle-cell and giant-cell sarcomas, endotheliomas, peritheliomas and angiosarcomas have been described, as well as fibromas and angiomas. A detailed histologic description of the disease and its sequelae is impossible.

Xeroderma pigmentosum presents such striking symptoms that it is readily recognized. The early date of onset and the limitation of symptoms to exposed surfaces, together with the combination of pigmented lesions, telangiectases, atrophic spots and areas, associated with the peculiar photophobia and lacrimation, are seen only in this affection.

Treatment is unsatisfactory. Life may be prolonged, however, by preventing exposure to the rays of the sun. General hygienic care is important. The malignant growths respond well to treatment with radium and roentgen rays. Surgery is often indicated.

In most cases the outlook is grave; however, with careful treatment life may be prolonged several years.

Other Precancerous Dermatoses

Arsenical keratoses develop in people who have used the drug over long periods for the relief of cutaneous dermatoses, such as psoriasis and dermatitis herpetiformis. They are usually associated with pigmentation. Multiple epitheliomas not infrequently develop on these keratoses. I have observed one case in which more than a dozen epitheliomas, both superficial and deep, developed among hundreds of keratoses and hyperpigmented lesions. The malignant transformation occurred chiefly on the hands, limbs and scrotum.

Keratoses occurring in tar and paraffin workers are often associated with acneform lesions and areas of dermatitis, together with scars, the previous site of epitheliomatous ulceration that healed spontaneously. Cancer from tar is an industrial disease that has been reported in England.

Chimney-sweep (soot) cancer, usually occurring on the scrotum, is only of historic and scientific interest here, since it has been seen chiefly in England and is reported rarely at present.

Roentgen-ray keratoses occur in chronic radiodermatitis and, unfortunately, are seen quite often. They occur in the skin of unprotected operators most frequently, but occasionally in others. They are usually associated with areas of atrophy and telangiectasia, and not infrequently undergo malignant transformation. Electrodesiccation, endothermy or excision is recommended for their removal.

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References

1. Montgomery, H. Precancerous dermatosis and epithelioma in situ. *Arch. Dermat. & Syph.* 39:387-408, 1939.
2. Dubreuilh, W. Des hyperkératoses circonscrites. *Ann. de dermat. et de syph.* 3S 7:1158-1204, 1896.
3. Eller, J. J. and Ryan, V. J. Senile keratoses and seborrheic keratoses. *Arch. Dermat. & Syph.* 22:1043-1060, 1930.
4. Hartzell, M. B. Some precancerous affections of the skin, more particularly precancerous keratoses. *J. Cutan. Dis.* 21:393-403, 1903.
5. Fordyce, J. A. Epithelioma of skin, benign and malignant. *Transactions of the XVIIth International Congress of Medicine*, London, 1913. Section XIII, Part 1. Pp. 1-14.
6. Freudenthal, W. Verruca senilis und Keratoma senile. *Arch. f. Dermat. u. Syph.* 152:505-528, 1926.
7. Hookey, J. A. Keratoma senilis and verruca senilis: a clinical and histopathologic study. *Arch. Dermat. & Syph.* 23:946-959, 1931.
8. Montgomery, H. and Dörffel, J. Verruca senilis und Keratoma senile. *Arch. f. Dermat. u. Syph.* 166:286-296, 1932.
9. Taussig, F. J. Leukoplakia and cancer of the vulva. *Arch. Dermat. & Syph.* 21:431-445, 1930.
10. Montgomery, H., Counseller, V. S. and Craig, W. McK. Kraurosis, leukoplakia and pruritus vulvae. *Arch. Dermat. & Syph.* 30:80-100, 1934.
11. Bowen, J. T. Precancerous dermatoses: a study of two cases of chronic atypical epithelial proliferation. *J. Cutan. Dis.* 30:241-255, 1912.
12. Nomland, R. Multiple basal cell epitheliomas originating from congenital pigmented basal cell nevi. *Arch. Dermat. & Syph.* 25:1002-1008, 1932.
13. Fournier, A. and Darier, J. Épithéliome bénin syphiloïde de la verge (épithéliome papillaire). *Bull. Soc. franç. de dermat. et syph.* 4:324-328, 1893.
14. Morrow: Eine verbesserte Methode der Behandlung gewisser Hautkrankheiten. *Arch. f. Dermat. u. Syph.* 18:261, 1886.
15. Darier, J. De la psorospermose folliculaire végétante. *Ann. de dermat. et de syph.* 2S 10:597-612, 1889.
16. White, J. C. A case of keratosis (ichthyosis) follicularis. *J. Cutan. Dis.* 7:201-209, 1889. Keratosis follicularis (psorospermose folliculaire végétante). *Ibid.* 8:13-20, 1890.
17. Bowen, J. T.: cited by White.[16]
18. Trimble, W. B. Observations on keratosis follicularis. *J. A. M. A.* 59:604-607, 1912.
19. Wende, G. W. Keratosis follicularis resulting in multiple epithelioma: report of a case. *J. Cutan. Dis.* 26:531-551, 1908.
20. Paget, J. On disease of the mammary areola preceding cancer of the mammary gland. *St. Bartholomew's Hosp. Rep.* 10:87-89, 1874.
21. Hartzell, M. B. Extramammary Paget's disease, with report of a case occurring on the forearm, associated with a nævo-carcinoma. *J. Cutan. Dis.* 28:379-388, 1910.
22. Montgomery, H. Superficial epitheliomatosis. *Arch. Dermat. & Syph.* 20:339-357, 1929.
23. Hebra, F. and Kaposi, M. *Lehrbuch der Hautkrankheiten.* Vol. II. 735 pp. Stuttgart: Ferdinand Enke, 1876. P. 182.

ACUTE TYPHOIDAL CHOLECYSTITIS AND CHOLELITHIASIS OCCURRING FORTY-THREE YEARS AFTER TYPHOID FEVER*

Report of a Case

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ACUTE suppurative cholecystitis has been recognized as a complication of typhoid fever since the report of a case by Gilbert and Girode[1] in 1890. In 1898, Cushing[2] pointed out that *Eberthella typhosa* may be responsible for the formation of gallstones. It is also well understood that persons may harbor *E. typhosa* in their biliary or intestinal tracts for many years and thus act as carriers of typhoid fever. Nevertheless, the occurrence of acute suppurative cholecystitis due to *E. typhosa* over forty years after the original attack of typhoid fever is sufficiently unusual to merit recording, and such a case is presented.

CASE REPORT

Mrs. F. F., a 64-year-old widow, entered the Medical Service of the Peter Bent Brigham Hospital on August 1, 1940, under the care of Dr. Reginald Fitz; she complained of pain in the right upper quadrant, nausea and vomiting of 2 days' duration. In 1897, the patient had typhoid fever, and several weeks later an attack of abdominal pain was diagnosed as typhoidal cholecystitis. In 1911, she was ill for 3 weeks with abdominal pain and jaundice. In 1926 and again in 1937, she suffered attacks of pain in the right upper quadrant of the abdomen, indigestion, nausea and vomiting. Intravenous cholecystograms in 1927 showed no definite gall-bladder shadow. Cholecystectomy was advised but was refused. There had been no further attacks of abdominal pain until 2 days before entry, when the patient complained of right epigastric pain and indigestion. These symptoms were at first relieved by soda, but the day before entry the pain became severer and radiated to the right shoulder. She became nauseated and vomited repeatedly. The bowels had moved twice since the onset, but their color was not noted. There had been no recent chills or jaundice. The patient had avoided fatty foods for many years, because they gave her indigestion.

Past history showed that the patient underwent subtotal thyroidectomy in 1925 for goiter with hyperthyroidism. She was in the hospital in June, 1940, because of bilateral bronchopneumonia. For 10 years she had had dyspnea on exertion.

There was no family history of typhoid fever, diabetes, tuberculosis, cancer or blood diseases.

Physical examination showed an extremely ill, markedly obese woman. The rectal temperature was 102°F., and the pulse rate was 140. The blood pressure was 145/60. There was marked spasm and tenderness over the entire right side of the abdomen, with maximum tenderness in the right upper quadrant. The tongue was covered by a heavy yellow coat. There were moist rales at both lung bases. The heart was not enlarged, and the sounds were regular and of good quality. Rectal examination was negative. Generalized arteriosclerosis was evident.

Blood examination showed a red-cell count of 4,200,000 with a hemoglobin of 85 per cent (Sahli). The white-cell count was 19,500 but gradually decreased to 8500. The blood smear showed 83 per cent polymorphonuclear leukocytes, 14 per cent lymphocytes, and 3 per cent monocytes. The icteric index was 11. Urinalysis was not remarkable except for a slight trace of albumin. The blood Widal reaction was positive in a 1:160 dilution of the serum. The results of cultures are summarized in Table 1.

TABLE 1. *Reports on Cultures.*

MATERIAL	DATE TAKEN	REPORT
Pus from abscess (at operation)	August 16	*Eberthella typhosa* (pure culture)
Pus from wound	August 28	*Staphylococcus aureus*
Bile from drainage tube	August 28	*E. typhosa* (pure culture)
Center of gallstone	August 29	*E. typhosa* (pure culture)
Urine	August 20	No growth
Urine	August 24	No growth
Urine	August 26	No growth
Duodenal washings	September 13	No growth
Stools (8 specimens)	August 20 to September 10	No enteric pathogens
Stool	September 12	*E. typhosa*
Stool	September 28	*E. typhosa*

The diagnoses were acute cholecystitis, generalized arteriosclerosis and obesity.

The patient was treated by bedrest and heat to the abdomen for 15 days before operation was undertaken. During this time, she ran an irregular fever up to 103.6°F. by rectum. In general, the fever and pulse rate tended to be lower after admission. Nausea and vomiting appeared intermittently. She was given digitalis because of the basal rales and the possibility of heart failure. The right upper-quadrant symptoms persisted, and 1 week after entry a tender mass about 8 by 8 cm. was palpable. The patient was frequently observed by Dr. Reginald Fitz and Dr. John Homans during her hospital stay, and it was their opinion that a perforation of the gall bladder had occurred and that drainage was indicated at that time. However, it was believed that the simplest procedure under local anesthesia should be performed, because the patient was very ill.

Cholecystostomy under local anesthesia was performed by Dr. John Homans on August 15, 1940. A single large gallstone, the size of a ripe olive, was removed. The gall bladder was inflamed and thickened except for one gangrenous area on the anterior medial aspect. Immediately adjacent to that portion of the gall bladder was an abscess walled off by omentum. From the abscess about 30 cc. of thick greenish-yellow pus was evacuated, from which *E. typhosa* was recovered in pure culture. A catheter was sewed in the gall bladder, and a drain was left in the abscess cavity.

After operation the patient's pulse and temperature

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showed a downward tendency so that by the 16th postoperative day they were within normal limits. Bile drained in amounts of 100 to 400 cc. daily from the cholecystostomy tube until it was removed on the 15th postoperative day. The drain was taken out 5 days after operation. The stools contained bile at all times, but no bile exuded from the wound after the tube was removed. The wound became secondarily infected in the region of the tube and drain, but otherwise healed quickly. The patient was out of bed 21 days after operation and went home 9 days later. She never became jaundiced, and her general condition was markedly improved at the time of discharge from the hospital.

Discussion

Because of their significance the classic observations of Cushing[2] in relation to typhoidal cholecystitis and cholelithiasis are repeated here. They are as follows:

> (1) The bacilli during the course of typhoidal infection quite constantly invade the gall-bladder; (2) the organisms retain their vitality in this habitat for a long period; (3) in the course of time the bacilli are almost invariably found to be clumped in the bile, suggesting the occurrence of an intravesical agglutinative reaction; (4) these clumps presumably represent nuclei for the deposit of biliary salts, as micro-organisms may with regularity be demonstrated in the centres of recently formed stones; (5) gall-stones being present in association with the latent, long-lived, infective agents, an inflammatory reaction in the viscus of varying intensity may be provoked at any subsequent period.

This patient had her initial attack of cholecystitis only a few weeks subsequent to recovery from typhoid fever in 1897. Four attacks of cholecystitis followed at irregular intervals, but it was not until forty-three years after the attack of typhoid fever that she was subjected to operation. The last attack was undoubtedly the severest, and was a true suppurative cholecystitis, with perforation of the gall bladder and formation of an extravesical abscess. The unabated virulence of the infective agent was demonstrated by the patient's stormy clinical course. It is difficult to describe how critically ill this patient was, but it will suffice to say that experienced observers watched her carefully for two weeks before advising even the simplest operative procedure.

The amazing vitality of the *E. typhosa* was only too well demonstrated here. After a forty-three-year interval, the organisms were recovered in pure culture from the bile, from the pus in the extravesical abscess and from the center of the gallstone. I have not found the report of any case in which *E. typhosa* was recovered from the center of gallstones so long after the original attack of typhoid fever. Whipple[3] mentions a case in which he recovered *E. typhosa* from the centers of three gallstones in a patient who had had typhoid fever thirty-two years previously.

Since the gall bladder was not removed in this case, no histologic study was possible. However, Mallory and Lawson[4] found that seven gall bladders from persons who were known to be typhoid carriers for three months to thirty years all showed evidence of chronic cholecystitis. These workers stated that the constant feature in the gall bladders was a diffuse lymphocytic and plasma-cell infiltration of the mucosa. In addition, there were dense focal collections of lymphocytes in typical lymph-node formation, with hyperplastic germinal centers of immature cells. No organisms could be demonstrated in the wall of any of the gall bladders, and there was no cholesterosis.

The patient in this case raised a large family and did all the cooking, yet she caused no known cases of typhoid fever. Undoubtedly she must have been discharging typhoid organisms in her feces for years, if only intermittently. Unfortunately, no stool cultures were made preoperatively. On ten occasions after the cholecystostomy tube was removed, stool cultures were made; only two were positive for *E. typhosa*. These positive cultures were the last of the series, and were taken fourteen and thirty days respectively after the bile ceased draining through the tube.

Because the patient was a poor operative risk, the gall bladder was not removed. Although drainage and removal of the stone have not cured her of being a typhoid carrier, the gall bladder is now free of a porous foreign body that contained *E. typhosa*, and in time the viscus may become sterile. At any rate, in this case it was probably wiser to have a living typhoid carrier than to risk an operative fatality by cholecystectomy.

Summary

A case of acute suppurative typhoidal cholecystitis and cholelithiasis occurring forty-three years after typhoid fever is reported.

Eberthella typhosa was recovered by culture from the bile, from the center of the gallstone and from the pus in the extravesical abscess. The patient was treated by cholecystostomy and removal of the single gallstone, because she was too poor an operative risk to undergo cholecystectomy. The typhoid organisms were still present in the stools forty-five days after operation.

References

1. Gilbert, A. and Girode, J. Contribution à l'étude bactériologique des voies biliaires. *Semaine méd.* 10:481, 1890.
2. Cushing, H. W. Typhoidal cholecystitis and cholelithiasis. *Bull. Johns Hopkins Hosp.* 9:91-95, 1898.
3. Whipple, A. O. The surgical treatment of bile typhoid carriers. *Ann. Surg.* 90:631-642, 1929.
4. Mallory, T. B. and Lawson, G. M., Jr. Chronic typhoid cholecystitis. *Am. J. Path.* 7:71-75, 1931.

CLINICAL AND LABORATORY OBSERVATIONS ON HEMOGLOBINURIA OCCURRING DURING SULFANILAMIDE THERAPY*

D. Rourke Gilligan, M.S.,† and Israel Kapnick, M.D.‡

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ACUTE hemolytic anemia following sulfanilamide therapy is not uncommon[1, 2]; Wood[1] has reported an incidence of 2.4 per cent of acute hemolytic anemia in 378 adults and of 8.3 per cent in 144 children treated at the Johns Hopkins Hospital. Hemoglobinuria associated with the acute hemolytic anemia has been reported, however, in very few cases. Thus in 21 cases of acute hemolytic anemia following medication with sulfanilamide, Wood[1] observed one with hemoglobinuria complicated by gross bleeding from a carcinoma of the bladder, and another in which there was hemoglobin in the plasma but no hemoglobinuria. Kohn[3] reported a case of hemoglobinuria in a baby, one year of age. Strasser and Singer,[4] Keefer[5] and Tavat and Shepard[6] have each described one case of hemoglobinuria in adults following therapy with this drug.

We have availed ourselves of the opportunity to make clinical observations, hematologic studies and quantitative studies of hemoglobinemia and hemoglobinuria in a case of hemoglobinuria associated with an attack of acute hemolytic anemia during sulfanilamide therapy, which occurred recently in the Beth Israel Hospital. A comparison has been made of the findings in this case with those in some other clinical conditions associated with hemoglobinuria.

Case Report

I. R., a 38-year-old Negro chauffeur, entered the hospital on February 5, 1940, with typical signs and symptoms of acute appendicitis. The body temperature was 100°F.; the white-cell count was 15,500; the spleen and liver were not palpable; the scleras were not icteric; the prostate was enlarged, with evidence of prostatitis. X-ray examination of the abdomen by flat plate was negative. There was a history of syphilitic infection 15 years before admission, for which some treatment had been received at that time, and a history of gonococcal infection 4 years before admission. On two examinations during the present admission the blood Hinton test was positive, the Kahn test doubtful, and the gonococcus complement-fixation test positive. Shortly after admission, an acutely inflamed appendix was removed under novocain spinal anesthesia. The postoperative course was essentially uneventful until the 4th postoperative day, when the temperature rose to 102°F. at noon and remained elevated to 100 or 101.5°F. for the following two days. There were slight redness and induration of the wound. Twenty grains of sulfanilamide and 20 gr. of sodium bicarbonate were administered orally every 4 hours for 2½ days. The dosage of sulfanilamide was then decreased to 60 gr. daily. During these 3½ days of sulfanilamide therapy, the temperature decreased to 99°F. (Fig. 1). At the end of this time, that is, on the 10th postoperative day, the temperature again increased to 100°F., and a slightly icteric tint of the scleras was noted. The red-cell count, which was 4,500,000 on the day after operation, had gradually decreased to 3,500,000 at this time; the blood hemoglobin had decreased from 88 to 72 per cent. The white-cell count was 24,900. Sulfanilamide was omitted. Eighteen hundred cubic centimeters of 10 per cent glucose in physiologic saline solution was given intravenously. Twelve hours later the red-cell count had dropped to 1,400,000, and the hemoglobin to 28 per cent; the scleras had become more icteric, and the temperature had risen to 103°F. The patient complained of no symptoms and said he "felt fine"; there were no chills, backache or abdominal cramps. At this same time he voided 500 cc. of dark, Burgundy-red, clear urine, containing no red cells or casts. The guaiac and benzidine tests were strongly positive. A quantitative study of the hemoglobin of this urine by the benzidine method[7] revealed 460 mg. of hemoglobin per 100 cc.

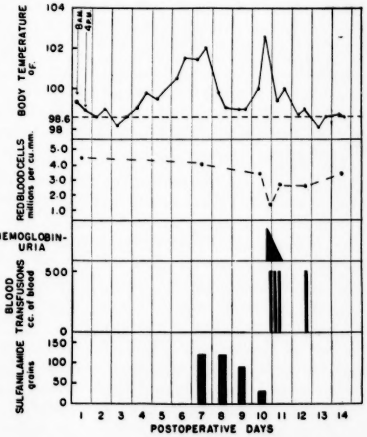

Figure 1. *Relation of Fever, Acute Anemia and Hemoglobinuria to Sulfanilamide Therapy.*

Three transfusions of 500 cc. of citrated blood were given in the following 12 hours; the red-cell count increased

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to 2,800,000, the hemoglobin to 54 per cent, and the temperature fell to 99.5°F. The white-cell count was 25,500. The spleen and liver were not palpable. Hemoglobinuria persisted for a total of 18 hours, during which the urine became progressively less red. One and a half days after sulfanilamide had been omitted, the temperature was normal, the plasma was slightly reddish and contained 25 mg. of hemoglobin per 100 cc., and the plasma bilirubin was 1.54 mg. per 100 cc. Urine voided a few hours after this plasma specimen was taken was normal in color and showed no albumin and no hemoglobin. There was no bile in the urine at any time. The following day the plasma was normal in color and contained a normal amount of hemoglobin, namely, 5 mg. per 100 cc. of plasma; the plasma bilirubin was 1.33 mg. per 100 cc.; the red-cell count was 2,800,000 and the blood hemoglobin 62 per cent. Another transfusion of 500 cc. of blood was given, and ferrous sulfate therapy was started. By the 4th day after the apparent onset of the hemolytic attack, the red-cell count was 3,500,000, the blood hemoglobin 70 per cent, the white-cell count 20,600 and the plasma bilirubin 0.3 mg. per 100 cc. The scleras no longer appeared icteric. Further convalescence was uneventful. The patient was discharged to the Out-Patient Department for follow-up study and treatment of syphilis.

The time between the beginning of sulfanilamide therapy and the development of the acute hemolytic attack in this case — namely, three and a half days — accords with the findings of others, who report these attacks as occurring between the third and seventh days of sulfanilamide therapy.[2, 5] The therapeutic dosage used was not excessive: Keefer[5] and Long and Bliss[2] have pointed out that there is no correlation between the size of the therapeutic dose and the development of an acute attack of anemia. On the other hand, certain subjects appear to be particularly susceptible to the development of these attacks, for the same patient has been shown to suffer a recurrence when a second course of the drug was administered.[1]

In the case described, hemoglobinuria occurred during the acute attack of hemolytic anemia. Hemoglobin first appeared in the urine about twelve hours after the temperature began to rise and the icteric tint of the scleras was noted; hemoglobinuria lasted eighteen hours and appeared to cease about simultaneously with cessation of blood destruction. In Kohn's[3] case hemoglobinuria lasted for twenty-four hours and in Strasser and Singer's[4] for three days. In our case the urines containing hemoglobin varied from dark Burgundy-red to pink, in Kohn's[3] case the urines were pinkish brown and reddish brown, and in Strasser and Singer's[4] case the urine was described as *bierbraune*.

No enlargement of the spleen and liver was discernible in the case of this study. In the case described by Strasser and Singer[4] the spleen became palpable, but the liver was not felt. Splenomegaly and hepatomegaly are only occasionally found in cases with the acute attacks of hemolytic anemia following the administration of sulfanilamide.[1, 2] On the other hand, splenomegaly is not uncommon in the slowly progressive type of anemia encountered more frequently with continued therapy using this drug.[5]

The absence in this case of symptoms such as chills, backache and abdominal pain, characteristic of attacks of intravascular hemolysis seen in the syphilitic type of paroxysmal hemoglobinuria and in attacks of hemoglobinuria following transfusion of incompatible blood, is noteworthy. Similarly, in the case described by Strasser and Singer[4] there were no symptoms except rather severe fatigue. In our case there was a rise in temperature and a marked leukocytosis; in Strasser and Singer's[4] there was a rise in temperature during the attack. It is to be noted that fever and leukocytosis during sulfanilamide therapy occur in acute attacks of hemolytic anemia unassociated with hemoglobinuria.[2, 5] Hemoglobinuria, unassociated with symptoms, and in fact in the absence of development of fever, is observed in attacks of march hemoglobinuria,[8] is frequently observed in the attacks in Marchiafava-Micheli disease[9, 10] and has been described in a case of massive hemoglobinuria of obscure etiology studied in this laboratory.[11]

Although acute hemolytic anemia during therapy with sulfanilamide and related drugs is usually not associated with hemoglobinuria, hemoglobinuria following these drugs apparently never occurs except during an attack of acute anemia. The hemolysis which gives rise to the hemoglobinuria and hemoglobinemia is probably only a small part of the total blood destruction occurring during the hemolytic attack. Comparison of the data in the case of the present study with that collected in other studies of hemoglobinuria made in this laboratory[7, 8, 11] strongly indicates that the amount of hemolysis represented by the circulating hemoglobin in the case of the present study was far too little to explain the rapid development of anemia. For example, the red-cell count decreased in twelve hours from 3,500,000 to 1,400,000, during which 2.3 gm. of hemoglobin was excreted in the urine, whereas in a case of intravascular hemolysis and hemoglobinuria of obscure etiology studied here,[11] the red-cell count decreased only from 4,700,000 to 4,200,000 in three days, during which a total of 16 gm. of hemoglobin was excreted in the urine. Similarly, in the case of the present study the plasma-hemoglobin concentration was only 25 mg. per 100 cc. eighteen hours after hemoglobinuria was first noted and was normal the following day, whereas the plasma-hemoglobin in the

other case remained elevated to levels of 500 to 300 mg. for the three days discussed. On the basis of previous findings concerning the rate of fall of plasma hemoglobin after a single intravenous injection of a solution of hemoglobin in normal persons,[7] it can be roughly estimated that the plasma hemoglobin was not greater than 1000 mg. per 100 cc. at the time of maximum hemoglobinuria, since it had decreased to 25 mg. in eighteen hours. This amount in 3000 cc. of plasma would be equivalent to only 30 gm. of hemoglobin, or the amount of hemoglobin in 190 cc. of normal blood. If the plasma hemoglobin did not suddenly reach such a peak and then decrease as after a single injection of hemoglobin in solution into the blood stream, but remained at an appreciably lower level than this peak for several hours during the hemolytic crisis, the amount of hemolysis still would not be essentially different from the value estimated.[11] Obviously many times this amount of hemolysis must have occurred to account for the acute development of the severe anemia. These considerations indicate that the mechanism of the development of the acute anemia following sulfanilamide therapy is probably the same in attacks associated with hemoglobinuria and in attacks in which this manifestation of hemolysis is not present. As suggested by Long and Bliss,[2] hemoglobinuria in attacks of acute hemolytic anemia following sulfanilamide may occur only in cases with exceptionally rapid hemolysis. A similar situation exists in congenital hemolytic icterus and acute hemolytic anemia (Lederer type), in which hemoglobinuria sometimes occurs in the fulminating hemolytic crises.[12]*

Because of the presence of syphilis, a Donath–Landsteiner test was performed on the blood of this patient two days after the beginning of the hemolytic attack, and was found to be negative. The red cells were not hemolyzed by the addition of small amounts of hydrochloric acid to the plasma as in the acid hemolysis test,[10] which is diagnostic of cases of Marchiafava–Micheli disease.[10] No hemolysis occurred on incubation of the patient's washed red cells suspended in physiologic saline solution containing sulfanilamide in concentrations ranging from approximately 10 to 50 mg. per 100 cc., or on incubation of the washed red cells suspended in the plasma of a patient of the same blood group who was receiving sulfanilamide therapy and had a plasma concentration of free sulfanilamide of 9.3 mg. per 100 cc. Tests made several weeks after the hemolytic attack failed to show hemolysis on incubation of the patient's washed red cells suspended in the plasma to which had been added acetylsulfanilamide to give concentrations ranging from approximately 6 to 30 mg. per 100 cc.

The treatment of cases developing acute hemolytic anemia during sulfanilamide therapy consists in immediate withdrawal of the drug, forcing of fluids, and repeated transfusions as indicated during the one to three days of the hemolytic attack. The treatment of these cases associated with hemoglobinuria is the same, except that sodium bicarbonate should be administered in sufficient amounts to keep the urine alkaline, so that the kidneys may be protected against damage due to deposition of hemoglobin pigment in the tubules.[5]

Summary

A case of hemoglobinuria occurring during an attack of acute hemolytic anemia following sulfanilamide therapy is reported. The hemolytic process was extremely rapid, the red-cell count decreasing from 3,500,000 to 1,400,000 in twelve hours. Hemoglobinuria appeared during the height of the attack and lasted for eighteen hours. There were fever, leukocytosis and jaundice during the attack but no symptoms, the patient insisting that he "felt fine." The hemolytic attack apparently lasted for about twenty-four hours, during which the patient was treated by blood transfusions. Quantitative data on plasma and urine hemoglobin indicate that the hemoglobin that gave rise to the hemoglobinemia and hemoglobinuria represented only a very small amount of the total hemolysis.

The mechanism of the development of the acute anemia during sulfanilamide therapy is probably the same in cases without hemoglobinuria as in cases in which this manifestation of hemolysis is present.

*Since this manuscript was submitted, we have studied another case of hemoglobinuria following sulfanilamide therapy. This patient, a sixty-year-old man, received sulfanilamide in moderate dosage in the treatment of lymphogranuloma inguinale. Hemoglobinuria began on the sixth day of sulfanilamide therapy and lasted forty hours. As in the case reported in the text, the attack was asymptomatic, but there was a rise in body temperature to 102°F., and leukocytosis. Jaundice and anemia developed rapidly; the urine and stool urobilinogen excretions were markedly increased. The fragility of the red cells in hypotonic saline solutions was strikingly increased at the onset of hemoglobinuria and returned to normal about fifteen hours later. Increased fragility in severe acute hemolytic anemia following sulfanilamide has been recorded also by Ham and Castle.[13] The highest plasma-hemoglobin concentration during the attack was 480 mg. per 100 cc. Spectrophotometric examination showed the presence of methemalbumin in the plasma, together with oxyhemoglobin; the urine, which was maintained alkaline throughout the attack, contained only oxyhemoglobin with no methemoglobin, hemoglobin casts or hemosiderin. Recovery from the anemia occurred following four blood transfusions and subsequent iron medication.

References

1. Wood, W. B., Jr. Anemia during sulfanilamide therapy. *J. A. M. A.* 111:1916-1919, 1938.
2. Long, P. H. and Bliss, E. A. *The Clinical and Experimental Use of Sulfanilamide, Sulfapyridine and Allied Compounds.* 319 pp. New York: Macmillan Co., 1939.
3. Kohn, S. E. Acute hemolytic anemia during treatment with sulfanilamide. *J. A. M. A.* 109:1005, 1937.
4. Strasser, A. and Singer, K. Ueber Prontosil-Hämoglobinurie und andere Sulfanilamid-Blutschädigungen. *Med. Klin.* 34:783, 1938.

5. Keefer, C. S. Sulfanilamide: its mode of action and side effects. *M. Clin. North America* **23**:1133-1148, 1939.
6. Tavat, S. and Shepard: Fatal hemoglobinuria due to prontosil. *Türk. tib. cem. mec.* **5**:300-305, 1939.
7. Gilligan, D. R., Altschule, M. D. and Katersky, E. M. Studies of hemoglobinemia and hemoglobinuria produced in man by intravenous injection of hemoglobin solutions. *J. Clin. Investigation* **20**:177-187, 1941.
8. Gilligan, D. R. and Blumgart, H. L. March hemoglobinuria. Studies of the clinical characteristics, blood metabolism and mechanism: with observations in three new cases and review of the literature. *Medicine* (in press).
9. Hamburger, L. P. and Bernstein, A. Chronic hemolytic anemia with paroxysmal nocturnal hemoglobinuria. *Am. J. M. Sc.* **192**:301-316, 1936.
10. Ham, T. H. Studies on destruction of red blood cells. I. Chronic hemolytic anemia with paroxysmal nocturnal hemoglobinuria: an investigation of the mechanism of hemolysis, with observations on five cases. *Arch. Int. Med.* **64**:1271-1305, 1939.
11. Altschule, M. D. and Gilligan, D. R. A case of acute massive hemoglobinuria of obscure etiology with jaundice and anemia, showing exacerbation of hemolysis on walking. Clinical and hematological studies, and measurements of the blood pigment metabolism. *Arch. Int. Med.* (in press).
12. Dameshek, W. and Schwartz, S. O. Acute hemolytic anemia (acquired hemolytic icterus, acute type). *Medicine* **19**:231-327, 1940.
13. Ham, T. H. and Castle, W. B. Studies on destruction of red blood cells: relation of increased hypotonic fragility and of erythrostasis to the mechanism of hemolysis in certain anemias. *Proc. Am. Philosoph. Soc.* **82**:411-419, 1940.

MASSACHUSETTS MEDICAL SOCIETY

PROCEEDINGS OF THE COUNCIL

Special Meeting, April 9, 1941

A SPECIAL meeting of the Council of the Massachusetts Medical Society was held in John Ware Hall, Boston Medical Library, 8 Fenway, Boston, on Wednesday, April 9. The meeting was called to order at 10:30 a.m. by the president, Dr. Walter G. Phippen, Essex South; 187 councilors were present (Appendix No. 1).

The Secretary *pro tempore* presented the record of the stated meeting of the Council on February 5, 1941, as published in the *New England Journal of Medicine*, issue of February 27. The President declared the record approved as published.

The Council then proceeded to consider the matters for which the meeting was called, namely, reports from the Committee on Medical Education and Medical Diplomas and the Committee to Consider New Officers and By-Laws, copies of which had been forwarded to all councilors on March 26.

Committee on Medical Education and Medical Diplomas

The report (Appendix No. 2) was presented by the chairman, Dr. John P. Monks, Suffolk. At the suggestion of Dr. Monks, the President ruled that Recommendations 1 and 3 be considered first, since they had little to do with the main body of the report, and then Recommendation 9, which was the kernel of the report.

Recommendation 1 was accepted by the Council, and Recommendation 3 was withdrawn by Dr. Monks.

Recommendation 9 was then discussed, sentence by sentence. In regard to (*a*), Dr. Reginald Fitz, Suffolk, suggested that the sentence in Section 1 of Chapter V relating to "special meetings of the censors" be deleted. After reading (*g*), Dr. Monks invited discussion concerning the phrase, "has practiced for a minimum of five years," adding that this was now interpreted by his committee as meaning "five years after graduation." The question as to how graduates of foreign medical schools should be treated was brought up, but discussion was deferred. After the presentation of (*o*) and (*p*), Dr. Charles C. Lund, Suffolk, suggested that having different time limits for the receiving of applications of graduates of approved and unapproved schools seemed unnecessarily complicated, and made a motion to amend the changes so that all applications should be received at the earlier date. The motion was seconded and carried.

In the discussion of Recommendation 9 as a whole, Dr. Michael A. Tighe, Middlesex North, asked for information in regard to the admission of graduates of foreign schools, as previously referred to in the presentation of (*g*). Dr. Monks replied that his committee had had no difficulty in determining the desirability of a physician who was well known in his native country, but that considerable difficulty had been experienced in passing judgment on recent graduates who had come to the United States either of their own volition or as refugees. He added that accurate information collected by the proposed local boards of membership would greatly assist his committee in making its recommendations. Dr. J. Harper Blaisdell, Middlesex East, moved that (*g*) be amended by adding after the words, "five years," the phrase, "in this state." The motion was seconded and, after considerable discussion, was lost. It was moved and seconded that Recommendation 9 be adopted, with the amendment in regard to dates; it was so voted.

It was subsequently and separately moved, seconded and voted that Recommendations 2, 4, 5, 6 and 7 be adopted.

Dr. Monks then inserted Recommendation 7*a*, which concerned the elimination of the sentence, "Special meetings [of the censors] may be held by order of the Council," in Section 1 of Chapter V, as previously suggested by Dr. Fitz. Its adoption was moved, seconded and approved.

Dr. Monks, at the suggestion of the treasurer, Dr. Charles S. Butler, Suffolk, amended the first sentence of Recommendation 8 to read:

> The fee of three dollars shall be paid to the district secretary by an applicant for fellowship for each examination or re-examination by the censors. This shall be sent promptly to the treasurer of the general society for deposit in the funds of the Society.

Recommendation 8, as amended, was adopted, as was Recommendation 10.

The last sentence in Recommendation 11 was changed by Dr. Monks, at the suggestion of Dr. Fitz, to read, "It shall revise the list of medical schools and colleges recognized by the Council annually, for approval by the Council." Recommendation 11, as amended, was adopted.

The changes covering the readmission of former members of the Society — Recommendations 12, 13 and 14 — were adopted without discussion.

After commending Dr. Monks's committee, and Dr. Monks in particular, for a very able piece of work, the President asked for a motion to accept the recommendations as a whole. This was made and seconded, and was so voted.

Committee to Study New Officers and By-Laws

The report (Appendix No. 3) was presented by the chairman, Dr. John Homans, Suffolk. He stated that the committee had attempted to get in touch with all the district societies to obtain their ideas in regard to the proposed executive committee of the Council. The consensus was that such a committee should be composed of a representative from each district. Dr. Homans then suggested, with the approval of the President, that the Council consider the changes proposed in Chapters III, IV and VI relative to the creation of an executive committee.

The additions to Sections 5 and 7 of Chapter III, having to do with the election of the member of the Executive Committee by the councilors of each district, were then considered. Some discussion arose concerning the word, "immediately," and it was finally voted to amend both sections by substituting "at or as soon as possible" for the word. The additions were adopted, as amended.

Section 10, an addition to Chapter IV, was then discussed. Dr. Homans said that in the second paragraph the word, "immediately," should be replaced by "at or as soon as possible," as was done in Sections 5 and 7 of Chapter III. The President stated that the last sentence in the first paragraph was unnecessary, and it was voted that the sentence be deleted. Dr. Monks suggested that "1941" in the first sentence of the second paragraph be replaced by "the first year of operation," the change being accepted by Dr. Homans and the President. The new section, as amended, was adopted.

The addition to Section 1 of Chapter VI was adopted, as were the recommendations, as a whole, dealing with the Executive Committee.

Dr. Homans then proceeded with the proposed changes necessitated by the appointment of an executive secretary. He said that the changes in Section 4 of Chapter VI merely define what the secretary of the Society must do and what he may assign to an executive secretary. It was pointed out that the first sentence in the eighth paragraph was a repetition of the second paragraph; the deletion of this sentence was accepted. In the discussion of Section 5 of Chapter VI, it was suggested that, in the first paragraph, "shall" be replaced by "may" in the first sentence, and "until his successor has been duly elected" be replaced by "at the pleasure of the Executive Committee" in the second. (Subsequent to the meeting, the first sentence was shifted and substituted for the fifth paragraph of Section 10 of Chapter IV, where it obviously belonged.) In commenting on the suggested changes, the President called attention to the fact that they merely permitted the Executive Committee to choose an executive secretary if it saw fit or if it were so instructed by the Council. The changes, as amended, were adopted. The President ruled that the proposed change in Section 1 of Chapter V did not require action.

The Council then adopted the recommendations of the committee as a whole.

It was moved, seconded and voted that the thanks of the Council be extended to Dr. Homans and his committee and that the committee be discharged from further duty.

Incidental Business

The President then attempted to carry out certain routine business of the Society. Dr. Brainard F. Conley, Middlesex South, raised the question whether this could be done, since the meeting had been called for a special purpose. The President ruled that such matters could be considered, but asked for opinions from ex-presidents of the Society. Dr. Channing Frothingham, Suffolk, and Dr. Walter P. Bowers, Worcester, concurred,

whereas Dr. Halbert G. Stetson, Franklin, and Dr. Charles E. Mongan, Middlesex South, dissented. Dr. Elmer S. Bagnall, Essex North, moved that the Council endorse the President's interpretation; this motion was seconded and carried.

Three restorations to fellowship (Appendix No. 4) were authorized by the Council, and new committees to consider the restoration of eleven former fellows (Appendix No. 5) were nominated by the President and approved by the Council. With the latter, Dr. Monks suggested that the committees be instructed to report to the Council at the May meeting, owing to the proposed changes in the by-laws; the President instructed the Secretary to notify the committees accordingly.

The appointment of Dr. Edwin D. Gardner, of New Bedford, to replace Dr. Ralph W. French, of Fall River, as a delegate to the annual meeting of the Rhode Island Medical Society was confirmed.

An increase in the Committee on Maternal Welfare from ten to fifteen members was authorized by the Council.

A letter from Mr. William W. McCarthy, of the National Shawmut Bank, relative to means of financing the costs of medical care, was referred to the Committee on Public Relations.

Dr. Fitz, as chairman of the Committee on Medical Preparedness, presented a resolution covering the deferment of medical students and interns (Appendix No. 6). This was adopted by the Council.

Dr. Bagnall presented a motion stating that each district representative on the Committee on Public Relations should be a councilor and also the chairman of the public-relations committee in his district society. The President stated that the Council had no power to pass such a rule, since the selection of local officers rests entirely in the hands of the members of the district society, but that it might be acted on as a sense-of-the-meeting matter. It was so moved and seconded, and the motion was passed.

Dr. William A. R. Chapin, Hampden, asked for information in regard to what should be done by the medical profession to counteract the ruling recently obtained by the federal government in its suit against the American Medical Association and certain subsidiary organizations. Dr. Tighe, by permission of the President, replied that the decision would be appealed and that no action should be taken until the matter was finally settled in the courts.

The meeting was adjourned at 1:32 p.m.

ROBERT N. NYE, *Secretary* pro tempore.

APPENDIX NO. 1

ATTENDANCE

BARNSTABLE
M. E. Champion
D. E. Higgins
W. D. Kinney
O. S. Simpson

BERKSHIRE
J. J. Boland
I. S. F. Dodd

BRISTOL NORTH
W. H. Allen
R. M. Chambers
F. H. Dunbar
W. H. Swift

BRISTOL SOUTH
G. W. Blood
R. B. Butler
E. D. Gardner
F. M. Howes
H. E. Perry
C. C. Tripp

ESSEX NORTH
E. S. Bagnall
R. V. Baketel
C. S. Benson
E. H. Ganley
H. R. Kurth
R. C. Norris
L. C. Peirce
G. L. Richardson
F. W. Snow
T. N. Stone
C. F. Warren
C. A. Weiss

ESSEX SOUTH
N. P. Breed
Loring Grimes
P. P. Johnson
B. B. Mansfield
W. G. Phippen
Horace Poirier
E. D. Reynolds
C. F. Twomey

FRANKLIN
W. J. Pelletier
H. G. Stetson

HAMPDEN
F. H. Allen
W. C. Barnes
W. A. R. Chapin
J. L. Chereskin
E. C. Dubois
G. L. Gabler
P. E. Gear
Frederic Hagler
G. D. Henderson
M. W. Pearson
A. G. Rice
G. L. Schadt
G. L. Steele

HAMPSHIRE
J. D. Collins
L. N. Durgin
L. B. Pond

MIDDLESEX EAST
C. R. Baisley
J. H. Blaisdell
Richard Dutton
E. M. Halligan
J. H. Kerrigan
K. L. Maclachlan
G. R. Murphy
R. R. Stratton

MIDDLESEX NORTH
R. L. Drapeau
F. L. Gage
G. A. Leahey
M. A. Tighe

MIDDLESEX SOUTH
C. F. Atwood
E. W. Barron
Harris Bass
G. F. H. Bowers
R. W. Buck
E. J. Butler
B. F. Conley
P. A. Consales
C. L. Derick
A. W. Dudley
F. W. Gay
H. G. Giddings
H. W. Godfrey
A. M. Jackson
A. A. Levi
A. N. Makechnie
R. A. McCarty
J. C. Merriam
C. E. Mongan
J. P. Nelligan
Dwight O'Hara
L. S. Pilcher
Max Ritvo
E. S. A. Robinson
E. F. Ryan
E. J. Sawyer
E. F. Sewall
H. W. Thayer
J. H. Townsend
Fresenius Van Nüys
W. S. Whittemore
Hovhannes Zovickian

NORFOLK
J. D. Adams
Carl Bearse
M. I. Berman
G. F. Blood

F. P. Denny
G. L. Doherty
D. G. Eldridge
H. M. Emmons
Susannah Friedman
David Gluntz
B. T. Guild
Morris Ingall
I. R. Jankelson
C. J. Kickham
C. J. E. Kickham
E. L. Kickham
D. L. Lionberger
D. S. Luce
D. L. Lynch
S. M. Saltz
D. D. Scannell
J. W. Spellman
M. H. Spellman
J. P. Treanor, Jr.
W. J. Walton

NORFOLK SOUTH

C. S. Adams
H. H. A. Blyth
H. A. Robinson

PLYMOUTH

J. E. Brady
P. B. Kelly
P. H. Leavitt
G. A. Moore
D. W. Pope

SUFFOLK

A. W. Allen
W. B. Breed
W. E. Browne
C. S. Butler
G. C. Caner
E. M. Chapman
M. H. Clifford
Lincoln Davis
R. L. DeNormandie
N. W. Faxon
G. B. Fenwick
Reginald Fitz
Channing Frothingham
Joseph Garland
John Homans
A. A. Hornor
H. A. Kelly
T. H. Lanman
C. C. Lund
H. C. Marble
G. R. Minot
J. P. Monks
Donald Munro
H. L. Musgrave
R. N. Nye
F. R. Ober
J. P. O'Hare
L. E. Parkins
L. E. Phaneuf
Helen S. Pittman
G. C. Shattuck
R. M. Smith
M. C. Sosman
Augustus Thorndike, Jr.
E. F. Timmins
Conrad Wesselhoeft

WORCESTER

Gordon Berry
W. P. Bowers
L. R. Bragg
E. B. Emerson
G. E. Emery
J. M. Fallon
E. L. Hunt
E. R. Leib
W. F. Lynch
A. W. Marsh
C. A. Sparrow
F. H. Washburn
R. P. Watkins

WORCESTER NORTH

E. A. Adams
H. C. Arey
J. J. Curley
T. R. Donovan
C. B. Gay
J. C. Hales
B. P. Sweeney

APPENDIX NO. 2

REPORT OF THE COMMITTEE ON MEDICAL EDUCATION AND MEDICAL DIPLOMAS

The Council at its meeting May 21, 1940, directed the Committee on Medical Education and Medical Diplomas to submit to it changes in the by-laws relative to the method of admission of the graduates of unapproved medical schools to the Society. While engaged in this task the committee thought that certain other matters not directly in line with the above purpose, but more or less related to it, should be included in the changes to be submitted. Following are the report and recommendations as submitted to the Council at its meeting on February 5, 1941. It was decided at that meeting that the report should be printed in full with appropriate comments, so that the whole matter might be more carefully considered at a special meeting of the Council to be called for that purpose. Explanatory comments for which the chairman of the committee is solely responsible have been inserted after each suggested change in the by-laws.

* * *

For several years among the applicants for fellowship in the Society the number of graduates of medical institutions not on the list recognized by the Council has been increasing. At present there are two groups of such graduates. One, and much the larger group, is composed chiefly of graduates of domestic institutions not recognized as medical schools by the American Medical Association. This group also includes a few American-born graduates of foreign medical schools, who have studied abroad, usually because they were not accepted by any recognized domestic medical school. There are a few foreign-born, foreign-educated physicians in this group who have migrated to this country, chiefly before 1937. The other group, much smaller than the first, is composed almost entirely of foreign-born graduates of foreign medical schools who are chiefly German and Jewish, but by no means exclusively either. Most of these physicians have migrated recently to this country primarily to escape political oppression. Almost without exception, they have had a good medical education and are of proved ability, often being older men of outstanding ability with international reputations.

The members of the Committee on Medical Education and Medical Diplomas are unanimous in believing that it is in the best interests of this Society to treat these two groups differently. The basis of this difference we believe should be whether or not an applicant has had an adequate medical education and enjoys a good professional reputation. With very few exceptions the members of the first group have had an inadequate education, those of the second an adequate one; and it is usually not difficult to distinguish between them. We believe that members of the first group should be admitted to membership only when there is ample positive proof that they can be regarded as truly desirable additions to the Society. At present, in the absence of evidences of undesirability other than an inadequate medical education, they are assumed to be desirable. We cannot agree with this attitude. We believe the members of the second group should become members of the Society as soon as they have been long enough in this country to have created definite favorable opinion in the minds of colleagues whose judgment would be commonly considered valuable.

The committee has been unable under the present system to evaluate adequately the desirability for fellowship of the majority of candidates appearing before it. Repeated attempts to gather information about the prospective candidates from the officers and fellows of the district societies have usually failed. A typical situation is for an applicant who is a graduate of an unrecognized domestic school to appear before the members of the committee, who have never seen him before, but who must decide as to his desirability from his appearance, diploma, application blank and a sheaf of letters personally solicited from his medical acquaintances, who invariably say that the applicant "is a capable and conscientious practitioner of medicine" and that his practice is "ethical." Only rarely has the committee received what it regards as a confidential expression of honest intelligent opinion regarding an applicant and his work from colleagues who really know him. Part of the present functioning of the committee as dictated by the by-laws has become farcical in the minds of its members. A major change in this undesirable situation seems impossible under the present by-laws.

The committee therefore recommends that the following changes be made in the by-laws:

1. The name of the committee be changed to the Committee on Medical Education. *(The Committee on Medical Diplomas was created in 1881 primarily to make a periodic revision of the list of medical schools recognized by the Council. The Committee on Medical Education was created in 1906 primarily to consider improvement of state laws regarding registration in medicine. The two committees were combined in 1913. The present chief function of the Committee on Medical Education and Medical Diplomas is to investigate the qualifications of applicants who are graduates of unrecognized schools. The change is recommended only in the interest of simplification.)*

2. *Chapter I, Section 1:* In line 5 on page 9 delete the clause, "that their names and addresses . . . prior to their examination by the censors." *(This clause appears more appropriately elsewhere. See Recommendation 9.)*

3. In line 10 on page 9 omit the words, "or college." *(It seems unnecessary now to use the terminology "medical school or college," though it once might have had some legal reason. The change is recommended only in the interest of simplification.)*

4. In line 14 on page 9 after "code of ethics of this Society;" insert "that they have made application according to the provisions of Chapter V, Section 2; that they have paid the examination fee of three dollars." *(The ultimate responsibility of seeing that all new applicants comply with the various provisions for entrance into the Society should rest with the censors. Article 3 of the constitution of the Society reads in part as follows, "No person shall become a member of the Massachusetts Medical Society except upon examination by the censors of said society . . . ." The contents of these two clauses are discussed under Recommendations 9 and 8a respectively.)*

5. *Chapter I, Section 6:* In line 5 on page 10 substitute the word, "December," for "November." *(The date of the present fall censors' examination is the first Thursday in November. According to the new "time-table" set up under Recommendation 9 the first Thursday in December seems better, as otherwise the closing date for applications from graduates of unapproved schools falls too close to Labor Day, an admittedly poor date for district secretaries and applicants alike. No such change in the date of the spring examination is needed.)*

6. *Chapter V, Section 1:* Beginning at line 11 from bottom of page 16, delete the whole paragraph, "Diplomas from medical schools . . . to take an examination." *(The contents of this paragraph appear more appropriately elsewhere. See Recommendation 9. The only factual change is in the period of time.)*

7. In line 2 from bottom of page 16 substitute the word, "December," for "November." *(See Recommendation 5.)*

8. At the bottom of page 16 insert the following: *(a)* "A fee of three dollars shall be paid by an applicant for fellowship to the district secretary for deposit in the funds of the general Society before each examination or re-examination by the censors. *(b)* An applicant shall not be considered as possessing the requisite qualifications for fellowship unless approved by at least three censors. *(c)* An applicant failing two examinations shall be disqualified from again applying for fellowship until three years have elapsed from the date of the last application."

(a. Examination by the censors of applicants for fellowship at present involves the applicant in no expense. The censors, however, are paid for their work, as provided for in Chapter V, Section 4, of the by-laws. In accordance with the usual custom of institutions of learning, learned societies and boards of registration in medicine everywhere it is felt that the Society should charge a fee for its examinations.

b. Unchanged.

c. If an applicant is not passed by the censors at two examinations, it is believed that some time should elapse before re-examination, so that an applicant may improve his qualifications and not appear at every examination with essentially unchanged qualifications.)

9. *Chapter V, Section 2:* To read as follows:

(a) "An applicant for fellowship who is a graduate of a medical school recognized by the Council shall apply on a form furnished for the purpose to the secretary of the district in which he has legal residence, not later than March 1 for the May censors' examination or October 1 for the December censors' examination. *(b)* At this time the district secretary shall verify the applicant's diploma and shall deliver the application form to the Secretary of the Society not later than March 10 or October 10 respectively. *(c)* An applicant nonresident in Massachusetts shall apply to the secretary of the Suffolk District Medical Society and shall be examined by the censors thereof. *(d)* Consideration of a late application shall be postponed until before the next succeeding examination. *(e)* The names of all such applicants, their addresses, medical schools, dates of graduation and the names and addresses of the various district secretaries shall be published in a list in the first number of the *New England Journal of Medicine* on or after April 1 or November 1. *(f)* Confidential communications regarding the qualifications of applicants for fellowship shall be requested of the fellows of the Society to be sent to the appropriate district secretary not later than April 15 or November 15.

(g) "An applicant for fellowship who is a graduate of a foreign medical school or a domestic medical school not on the list recognized by the Council or of a medical school no longer in existence, and who has practiced for a minimum of five years, shall apply for fellowship in like manner with the following exceptions and additions:

(h) "The application form must be submitted to the district secretary not later than February 15 or September 15. *(i)* At this time also the applicant must submit the name and address of a fellow of the Society who has agreed to act as his sponsor. *(j)* The sponsor's duty is to obtain from fellows of the Society who are acquainted with the applicant and his work, confidential written opinions regarding his qualifications for fellowship to be mailed directly to the district secretary not later than March 15 or October 15. *(k)* The application form of such an applicant shall be delivered by the district secretary to the Secretary of the Society not later than February 20 or September 20. *(l)* A list, similar to that of applicants who are graduates of recognized schools, but with the addition of names and addresses of sponsors shall be published in the first number of the *New England Journal of Medicine* on or after March 5 or October 5.

(m) "The president, secretary and supervising censor of the district society, sitting as a local board of membership, shall then gather such further information as is deemed necessary to determine whether an applicant is a capable and conscientious practitioner of medicine and possesses a good professional reputation among his col-

leagues. *(n)* Every candidate must be personally interviewed by this board.

(o) "The district secretary shall deliver to the chairman of the Committee on Medical Education a complete confidential file of all applications including correspondence, and the written recommendations of the local board with supporting reasons for advocating the acceptance or refusal of each applicant not later than April 1 or November 1. *(p)* The committee shall then determine whether or not each candidate shall be approved for examination by the censors, and shall notify the district secretary and each applicant of their decision not later than April 20 or November 20."

(a. Provisions unchanged except for dates. The system of definite unchanging dates from year to year is utilized throughout except in the case of examination dates, rather than the present method of dating by giving the number of weeks before the examination. The present method has always caused confusion in the minds of district secretaries and applicants alike since the actual date differs each year. Dates are set so to allow ample time for the district secretaries, the secretary of the Society, the editor of the Journal, *the local boards of membership and the Committee on Medical Education to perform their duties properly, as well as to allow no misunderstanding in anyone's mind concerning the date by which certain duties should be finished. Anyone who has not been one of the abovementioned officers has difficulty in appreciating the importance of this point.*

b. Transporting bulky framed diplomas to be shown to more than one official of the Society, as now occurs, is unnecessary. The Secretary of the Society has to verify and edit certain information on the application blanks before publication in the Journal.

c. Unchanged.

d. Nothing is more troublesome to all the officials concerned than attempting to handle late applications, which now are submitted up to the very eve of the examination and which are always coupled with requests for special consideration.

e. Unchanged except as to dates.

f. Occasionally unfavorable information of importance about an applicant exists. If it is withheld by an applicant's colleagues and an applicant is admitted to the Society, responsibility should rest on those who withheld the information. Such information when made available is always treated confidentially.

g. Unchanged in essentials.

h. The difference in dates from those in a *is due to the more numerous procedures required in the cases of graduates of unapproved schools.*

i and *j. Sponsorship of an applicant who is a graduate of an unapproved school is a new proposal. Previously the applicant always personally approached his colleagues and asked for written recommendations. This system produced recommendations some of which were retracted by their writers in separate communications, and other recommendations which were obviously written by fellows who were only casually acquainted with the applicant, and others which were refuted by other available information. It is hoped that the new system will alleviate the embarrassment of an applicant's personally asking for a recommendation from a fellow who does not feel he can honestly give it.*

k. See b.

l. Unchanged, except as to dates.

m. This change is the most fundamental of all those suggested. The Committee on Medical Education and Medical Diplomas has sensed for a long time how helpless it was in obtaining adequate information on which to determine the desirability of candidates for fellowship; this point has already been discussed more fully in the formal report. It is believed that a local board will be in every way better fitted to obtain this information than the central committee. The number of men on the board is small, they are already in positions of responsibility in their local society, and two of the three are already members of the board of censors, which eventually will examine those candidates finally approved. Further, it is very definitely felt that in the case of graduates of unrecognized schools the essential responsibility of whether or not they should be admitted to membership in the local society should lie with their own nearby colleagues, not with those farther afield. See Recommendation 11 e.

n. Unchanged, except that the interview shall be carried out by the local board rather than the central committee.

o and p. *This provides that the central committee shall take the responsibility of seeing that on one hand undue pressure has not been brought to bear on the local board to recommend for approval an undesirable applicant, nor on the other hand has unwarranted local prejudice barred from approval a desirable applicant.)*

10. *Chapter V, Section 3:* In line 4 on page 17 after the words, "applicants for fellowship," insert the clause "they shall see that each applicant pays the examination fee." *(See Recommendation 8* a. *This is inserted as it becomes a new duty for the district secretary.)*

11. *Chapter VII, Section 5:* First two paragraphs to be changed to read as follows:

(a) "The Committee on Medical Education shall consist of five fellows. It shall consider all matters relating to medical education which may be referred to it by the Council. *(b)* It shall review the case of every applicant for fellowship who presents according to the provisions of Chapter V, Section 2, a diploma from a medical school not on the list recognized by the Council. *(c)* It shall have the power to approve for examination by the censors such an applicant, and all decisions of the committee thereon shall be final. *(d)* It shall revise the list of medical schools recognized by the Council whenever it appears necessary."

(a. Unchanged.

b. Changed in accordance with 9 o *and* p.

c. Unchanged.

d. Changed in that previously the committee had to await direction by the Council to accomplish this duty. It is believed that this list should conform to that of the medical schools approved by the American Medical Association, which is changed from time to time. The present list dated 1934 needs sixteen changes to bring it into such conformity.)

A recent ruling by the President reversed the previous interpretation of the provisions of the by-laws regarding the application for readmission to the Society of a former fellow whose resignation had been requested by the Committee on Ethics and Discipline. Inasmuch as the individual in question was a graduate of an unrecognized school, it was ruled that he had to appear before the Committee on Medical Education and Medical Diplomas for approval, before being allowed to appear before the censors. Due to information requested from the chairman of the Committee on Ethics and Discipline, the Committee on Medical Education and Medical Diplomas disapproved the application. The latter committee, as a result of this case, believes that it should have no jurisdiction in such cases

of readmission to the Society, and as a result studied the provisions of the by-laws regarding readmission. With the approval of the Committee on Ethics and Discipline and the Committee on Membership it recommends that the following changes be made in the by-laws:

12. *Chapter I, Section 7:* To read as follows: "The resignations of fellows whose assessments have been paid in full or remitted may, on recommendation of the Committee on Membership, be accepted by the Council and sent to the treasurer of the Society." *(The sentence dealing with readmission is deleted. The matter is now dealt with in Recommendation 14* a.*)*

13. *Chapter I, Section 8:* Omit last paragraph, "Fellows who have been deprived . . . secretary of the general Society." *(The sentences dealing with restoration to fellowship are deleted. The matter is now dealt with in Recommendations 14* a, b, c, d, *and* e.*)*

14. *Chapter I:* Add *Section 10,* to read as follows:

(a) "Former fellows who desire to be readmitted to the Society shall make application in writing addressed to the Council and sent to the secretary of the Society. *(b)* Such applications shall be referred for investigation and personal interview to the local boards of membership, which shall report their recommendations to the Committee on Membership. *(c)* The committee shall render the final decision as to whether to recommend to the Council the readmission of former fellows. *(d)* The Council shall have the power to readmit former fellows so recommended. *(e)* Boards having under consideration the applications of fellows whose resignations have been requested by the Committee on Ethics and Discipline, or who have been deprived of fellowship under the terms of section 8, clause *(c),* shall consult with the Committee on Ethics and Discipline before reporting their recommendations."

(a *and* b. *The distinction formerly made in Chapter I, Sections 7 and 8, between the method used in readmitting to fellowship those fellows who having "resigned" and those who having been "deprived of the privileges of fellowship" desire to rejoin the Society has been eliminated. It is believed that the local boards of membership can more adequately investigate the facts surrounding a fellow's separation from the Society and the altered situation that leads him to seek readmission than can either the censors or a specially appointed committee, as is the practice at the present.*

c. *The Committee on Membership should retain jurisdiction to review the recommendations of the local boards as it does at present in all cases of deprivation of fellowship. At the present it has no jurisdiction in cases of readmission to the Society following resignation.*

d. *The Council should have the full power of readmission of all former fellows recommended by the Committee on Membership. At present it has no jurisdiction in cases of readmission to the Society following resignation.*

e. *At present in cases where the Committee on Ethics and Discipline has requested a fellow's resignation as a form of discipline, and such resignation has been received, and the fellow later reapplies for readmission, the Committee on Ethics and Discipline has no jurisdiction in the matter of readmission. If the fellow in question is a graduate of an unrecognized school he must appear at present before the members of the Committee on Medical Education and Medical Diplomas, who if they approve his application pass him on to the censors for examination. This procedure is most illogical, since those who know nothing about the fellow deal with his readmission, while those who know everything about him have no official hand in the matter. At present the Council acting on separate reports of the Committee on Ethics and Discipline and the Committee on Membership may deprive a fellow of the privileges of fellowship as provided in Chapter I, Section 8 (c). With such a fellow desiring restoration to fellowship, a special committee is appointed to consider his case, and the by-laws provide that this committee must include at least one member of the Committee on Ethics and Discipline. The latter committee believes that with the institution of local boards of membership consultation with the Committee on Ethics and Discipline will provide sufficient opportunity for the board to know all the facts in the case before reporting its recommendations.)*

JOHN P. MONKS, *Chairman.*

APPENDIX NO. 3

REPORT OF THE COMMITTEE TO CONSIDER NEW OFFICERS AND BY-LAWS

Following the Council meeting of October 2, 1940, a committee was appointed by the president of the Massachusetts Medical Society to study the desirability of establishing the offices of president-elect and full-time or executive secretary and to suggest the necessary changes in the by-laws required to create these positions. At the Council meeting of February 5, 1941, the by-laws dealing with the creation of the office of president-elect were accepted. At the same meeting the plan of having an executive secretary was accepted in principle, but the manner of electing the executive secretary was left to be determined.

At the Council meeting of October 2, 1940, a motion was made that this same committee should study the possibility of redistricting the Massachusetts Medical Society, with the idea of harmonizing its set-up with that of the American Medical Association and other state societies. The committee, in reporting at the Council meeting of February 5, 1941, took no action in respect to the problem of redistricting, but did suggest certain by-laws by which an executive committee of the Council could be established. In respect to the latter, the Council voted "that the committee continue and that it explore the possibilities of an executive committee so constituted that each district medical society would be represented."

Hence, your chairman has circularized the secretaries of the different district societies, asking them to secure, if possible, in the brief time between Council meetings, an opinion from their respective districts as to the best method of selecting an executive committee of the Council, and the possibility of redistricting the Massachusetts Medical Society.

In one way or another, your chairman has heard from six secretaries and from various sources has received the following impression: that no district desires a change in its boundaries and that a majority of the districts are opposed to such a change; that the idea of an executive committee of the Council is generally acceptable and that the districts prefer that each of them should be represented on this committee, no others to be made members of the committee except the officers of the Society. In accordance with this understanding, your committee, after consulting together, suggests the following changes in the by-laws.

JOHN HOMANS, *Chairman.*

CHAPTER III

District Societies

Section 5. (Additional)

The councilors of each district society shall meet immediately after the annual meeting of the district society in 1941 and elect one of their number to serve as a member of the Executive Committee of the Council in accordance with Chapter IV, Section 10. Thereafter, in a similar manner, they shall elect a new member from time to time.

Section 7. (Additional)

The secretary of each district society immediately after the annual meeting of the district society in 1941 shall call together its councilors for the purpose of electing a member of the Executive Committee of the Council and shall send the name of the member chosen to the Secretary of the general Society. He shall see that a new member is chosen in a similar manner to fill a vacancy as it occurs, in accordance with Chapter IV, Section 10.

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CHAPTER IV

The Council

Section 10. The Executive Committee shall consist of the President, President-Elect, Vice-President, Secretary and Treasurer *ex officiis*, and a councilor from each district medical society chosen in accordance with Chapter III, Section 5. The election of a councilor to the Executive Committee of the Council shall not be considered as leaving a vacancy among the councilors from the district he represents.

The councilors of each district society shall meet immediately after its annual meeting in 1941, as specified in Chapter III, Section 5, and in a similar manner at stated intervals as specified below, to choose one of their number to serve as a member of the Executive Committee of the Council.

A member of the Executive Committee shall serve for three years and shall not be eligible for re-election before the expiration of three years following the conclusion of his term of office; except that in 1941 six members shall be selected by lot to serve one year, six members shall be selected by lot to serve two years and six members shall be selected by lot to serve three years. Thereafter, six members shall be elected every year to succeed in office those whose terms are about to expire.

The Executive Committee shall meet at the call of the President at least once in each interval between Council meetings and may meet more often at the pleasure of the President. It shall assist the President in preparing for the consideration of the Council matters calling for action by the Council at its next meeting. It shall authorize action by the officers of the Society when circumstances require it, subject to the approval of the Council. It shall perform such other duties as the Council may require.

The consent of the Executive Committee shall be required to confirm the appointment, upon nomination by the President, of the Executive Secretary of the Society.

Upon request, members of the Executive Committee shall be paid the amount of their traveling expenses from the funds of the Society.

CHAPTER V

Censors and Supervisors

Section 1. The supervisors, representing the censors of the several district societies, shall constitute a board, which shall meet annually on the day appointed for the annual meeting of the Council. The board shall elect a chairman, who shall have power to call special meetings. Five supervisors shall constitute a quorum. The Secretary or Executive Secretary of the general Society shall act as secretary of the board. He shall call special meetings at the request of five supervisors. He shall keep a permanent record of the proceedings of the board, and shall provide, at the expense of the Society, papers and forms necessary for conducting examinations of applicants for fellowship. The board at its annual meeting shall adopt a uniform plan for the examination of applicants. The supervisors shall be paid the amount of their traveling expenses from the funds of the Society.

CHAPTER VI

Officers

Section 1. (Additional)

He shall call at least one meeting of the Executive Committee of the Council between Council meetings and may call more meetings if he so desires.

Section 4. The Secretary may assign to an Executive Secretary any or all the duties now to be enumerated, except as specified below:

The Secretary shall attend all meetings of the Society and of the Council, and shall record their respective proceedings in separate record books; and this duty he may not assign.

He shall cause to be engrossed and shall sign the diplomas of new fellows if satisfied that they have met the requirements of Sections 1 and 2 of Chapter I, and shall issue all diplomas and certificates of fellowship. He shall notify individual fellows, in appropriate instances, of votes by the Council granting permission, as the case may be, to retire, to resign, to change district membership, to have dues remitted, or of votes depriving them of the privileges of fellowship; and these duties he may not assign.

He shall act *ex officio* as secretary of all boards of trial; and this duty he may not assign.

He shall have custody of the seal of the Society and of all books, papers, manuscripts, prints and paintings belonging to the Society, except such as are in charge of the Treasurer; and this duty he may not assign.

He shall act *ex officio* as secretary of the Board of Supervisors and of the Committee on Publications and the Committee on Ethics and Discipline, and shall keep the records of each in a separate volume. He shall have custody of all records as thus kept.

He shall issue notices of the meetings of the Council. One month before the annual meeting of the Society, he shall issue to every fellow a program, which shall contain notification of the time and place of the annual meeting, notification of the stated meetings of the Council for the year and the meetings of the boards of censors, and information concerning the payment of assessments and the distribution of publications.

He shall record the Proceedings of the Council and of the Society. He shall keep a complete list of the fellows of the Society, with their addresses so far as known. He shall transfer fellows from one district to another under the terms of Chapter III, Section 2, and shall report to the Society at its annual meeting the changes in membership of the Society during the year.

He shall conduct the official correspondence of the Society, and shall notify officers, delegates and members of the committees of the general Society of their appointments and of their duties.

Under the direction of the Committee on Publications he shall issue at such intervals as may be determined by

the Council a directory of officers and fellows of the Society, which shall be furnished upon request to fellows who are not in arrears.

He shall perform such other duties as the Society or the Council may require.

Section 5. An Executive Secretary shall be chosen by the Executive Committee of the Council upon nomination by the President. He shall hold office until his successor has been duly elected.

He shall perform such duties as are assigned to him in Section 4 of this chapter and by the Executive Committee. In general, he shall assist the officers of the Society and such standing and other committees as may request his services, and the Society shall have the first call upon his services.

He shall attend all meetings of the Council and, on request, attend the meetings of the Executive Committee of the Council, but shall not vote in either.

An Executive Secretary need not be a physician.

APPENDIX NO. 4

Reports of Committees to Consider Petitions for Restoration to the Privileges of Fellowship

Restoration to fellowship, with the usual provision regarding payment of dues, was recommended for the following three former members:

Julian C. Gant, Arlington (Committee: Edwin P. Stickney, Letitia D. Adams and Alfred Weller).

Charles H. Hogan, Salem (Committee: Charles L. Curtis, Thomas F. Henry and Stuart N. Gardner).

Arthur J. Taveira, New Bedford (Committee: Frank M. Howes, Edwin D. Gardner and Curtis C. Tripp).

APPENDIX NO. 5

Committees Appointed to Consider Applications for Restoration to Fellowship

The following committees were appointed to consider the petitions for restoration to fellowship of the following eleven former members:

For Bernard H. Appel, Brighton:
Max Ritvo, David Stern and Robert H. Aldrich.

For Harold I. Cohen, Lynn:
Charles F. Twomey, Bernard Appel and Charles L. Hoitt.

For Frederick E. Cruff, Norwell:
Bradford H. Peirce, Roy F. Littlehale and Charles Hammond.

For J. Frank Curtin, North Abington:
Joseph H. Dunn, John M. Peckham and Jonah Fieldman.

For Leroy S. Ford, Keene, New Hampshire:
Samuel N. Vose, Hollis L. Albright and Walter H. Lacey.

For Maurice Gerstein, Brookline:
Charles J. Kickham, Edward L. Kickham and Albert Ehrenfried.

For Elihu I. Lewis, Boston:
William T. O'Halloran, Mark D. Altschule and Nathan L. Fineberg.

For Coval H. Liverpool, West Somerville:
Charles W. Finnerty, John E. Gillis and Herbert Cholerton.

For John L. O'Toole, Haverhill:
William W. Perrin, Lucien R. Chaput and George J. Connor.

For Nathan Silverman, Lawrence:
John J. Deacy, John J. Kelleher, Jr., and Joseph A. Levek.

For Thomas V. Uniac, Lawrence:
Roy V. Baketel, Victor A. Reed and Henry F. Dearborn.

APPENDIX NO. 6

Resolution Presented by the Committee on Medical Preparedness

Whereas, The regulations of the Selective Service Act provide against deferment for military training of particular groups of persons; and

Whereas, These regulations provide for individual deferment of persons in any capacity deemed necessary for the national health, safety or interest, thus enhancing the efficiency of such individuals for a particular type of such needed service; and

Whereas, Physicians play an indispensable part in both the civilian and military aspects of the national defense program; and

Whereas, The needs for competently trained physicians will be greatly extended to meet both the civilian and military requirements of the present emergency; and

Whereas, A period of four years of intensive continuous training is required after a man enters a medical school and thereafter at least one year of hospital experience as an intern before he can be developed into a physician of any competence; and

Whereas, The Council of the Massachusetts Medical Society here records as its considered opinion that the future health needs and proper medical care of the nation and of the defense forces demand that there be no interruption in the stream of adequately trained physicians entering the ranks of the profession from medical schools and hospitals; therefore, be it

Resolved, That the Council and members of the Massachusetts Medical Society urge local and appeal selective-service boards in Massachusetts to give due and proper consideration to the medical needs of their respective communities when considering physicians for military service, to the end that the citizens of rural sections and small towns be not deprived of necessary health and medical services; and be it further

Resolved, That, to ensure a continuing supply of adequately trained physicians to meet the nation's medical needs of the future, the Council and members of the Massachusetts Medical Society urge local and appeal selective-service boards carefully and sympathetically to consider semiannual deferments on an individual basis, as provided in selective-service regulations, of students in recognized schools for medical teaching and of interns in hospitals until the completion of at least one year's internship; and be it further

Resolved, That copies of this resolution be sent to the Governor of the Commonwealth of Massachusetts, to directors of the federal and state selective-service system, and to the chairmen and members of all local and appeal selective-service boards within the Commonwealth.

Reginald Fitz, *Chairman.*

MEDICAL PROGRESS

BACTERIOLOGY*

The Significance of Bacteriologic and Immunologic Procedures in the Diagnosis and Treatment of Infections

CHARLES A. JANEWAY, M.D.†

BOSTON

WITH the development of powerful and specific agents for the treatment of infections, accurate diagnosis has become increasingly important. It is extremely difficult to handle a patient in diabetic coma without the aid of a chemical laboratory, and it is equally impossible to give satisfactory care to patients with serious infections without the assistance of a good bacteriologic laboratory. Consequently, the efforts of the Massachusetts Department of Public Health to improve the quality of bacteriologic work throughout the Commonwealth by a system of inspection and approval of laboratories is commended. With these considerations in mind, I shall discuss the present status of diagnostic procedures from the point of view of both the clinician and the laboratory man.

BACTERIOLOGIC PROCEDURES

Smears

With the refinement of laboratory methods, older and simpler tests are often forgotten. This has been true of the practice of examining stained smears of bacteriologic material. As a method of exact diagnosis, a smear has great limitations, but as a guide to the clinician and bacteriologist, it is of inestimable value. It gives a tentative indication of the type of infection in a few minutes, whereas cultures take at least eighteen hours, and it shows the proportions of various types of organisms in mixed infections, as well as the cellular reaction in the exudate.

Smears are particularly useful in the examination of exudates from sites normally sterile, such as serous cavities, the subarachnoid space and tissues. The importance of smear examination in cases of peritonitis and empyema cannot be overemphasized, for cultures from these cases often fail to grow. A discussion of the valuable information yielded by smears of abdominal fluid obtained at laparotomy has recently been published.[1]

Smears made from sites at which there are normally profuse bacterial flora are difficult to interpret and usually fall to the lot of the medical man. Throat smears are extremely unreliable in the diagnosis of diphtheria and various forms of tonsillitis, and the physician should be guided by his clinical judgment from the appearance of the lesion and by properly taken cultures for confirmation. In pneumonia, the gross inspection of the sputum, in conjunction with examination of a stained smear, may yield valuable information, particularly in such unusual cases as Friedländer's pneumonia. In venereal diseases, smears may be very useful from a man, who normally has an almost sterile urethra, whereas those from the female cervix mean little unless frank pus is seen. Smears of urinary sediment are often more valuable than cultures, when the latter are done by simple broth inoculation. Perhaps the greatest use for smears in medical conditions is in examination of fluid aspirated from acutely inflamed joints, and of cerebrospinal fluid.

Certain pitfalls in smear examination are not commonly appreciated. All the gram-positive cocci — staphylococcus, pneumococcus and hemolytic streptococcus — tend to assume a diplococcal form when growing rapidly in the body, so that the finding of diplococci or short chains is not pathognomonic of a particular coccus, and one must accordingly be somewhat cautious in interpretation until cultures are made. Moreover, virulent hemolytic streptococci form capsules in rapidly spreading infections. In a case of peritonitis, recently observed, a smear showed gram-positive diplococci. These were taken to be pneumococci, and a Neufeld test was set up with Type 1 antipneumococcus serum. This showed large, apparently swollen capsules and was called positive. On the next day, culture revealed a pure growth of beta-hemolytic streptococcus, much to the bacteriologist's surprise.

Smears of the cerebrospinal fluid in meningitis may be quite confusing unless the physician is on his guard. The gram-positive cocci can be quite readily seen, but gram-negative meningococci may be very difficult to find. In children, meningitis due to the Pfeiffer bacillus (*Haemophilus influ-*

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enzae) is the commonest endemic form.[2] These organisms are frequently mistaken for meningococci by an inexperienced observer, because they may appear as gram-negative diplococci. They take stains with difficulty, and if *H. influenzae* infection is suspected, the smear should be stained with safranine for five or ten minutes, after which time the organisms will appear as quite small, very pleomorphic, gram-negative bacilli and cocci, often paired. Their early identification is essential, since specific rabbit-serum therapy offers the greatest hope in this highly fatal disease.[3, 4]

Cultural Methods

Taking cultures. To obtain positive cultures from patients with infections, intelligent cooperation between the physician and his laboratory associates is needed. Swabs must be taken from the lesion itself, with as little contamination as possible. This is particularly true in throat cultures, when the results vary enormously with the technic of the person taking the cultures. It is hardly necessary to point out that swabs must be kept moist and planted as soon as possible, because most pathogenic organisms die more quickly than their saprophytic companions. Various technics have been devised for keeping the swabs moist and the organisms alive. If the material can be kept cold, dropping the swab in a tube of broth is a good policy. A few drops of physiologic saline solution or water in the bottom of the tube with the swab suspended a little above it may help. Never dip swabs in saline solution, since it is quite toxic for most organisms. An English worker devised an excellent scheme for meningococcus-carrier studies, which laboratories serving practitioners might well adopt. The bottom of the test tube is filled with a small amount of blood agar on which the swab is allowed to rest.[6] As a general rule, all specimens do best if they are maintained at a temperature just above freezing during transport to the laboratory, rather than at warmer temperatures. This is particularly true of stool specimens, in which overgrowth of colon bacilli at room temperature will obscure the presence of a few pathogens.

Partial tension. A few tricks in the isolation of pathogenic organisms make a great difference. A slight increase in the carbon dioxide tension of the atmosphere stimulates the growth of bacteria. Furthermore, moisture has a marked effect, many organisms growing readily on fresh moist plates, and very poorly on old dry ones. The moisture can be conserved by covering the space between the Petri dish and its cover with Scotch tape or Parafilm, or by placing the Petri dishes in a museum or preserve jar, with moist blotting paper in the bottom and with a tightly fitting lid. Increased carbon dioxide tension can be secured in an individual plate culture by putting a small piece of carbon dioxide snow in the Petri dish cover, inverting the plate over it and sealing. For a group of plates in a jar, proper atmospheric conditions may be achieved by including several plates inoculated with *Bacillus subtilis*, as recommended by Fothergill and Sweet,[6] or by lighting a candle in the jar and clamping the lid on tightly, as recommended by Nye and Lamb.[7] I have found the latter method most convenient, because of its simplicity. The candle uses up a portion of the available oxygen, and produces water vapor and carbon dioxide; the last increases to about 3 per cent before smothering the flame, thus providing optimal conditions for the growth of such organisms as the meningococcus, gonococcus, *Streptococcus viridans*, hemolytic streptococcus, pneumococcus and staphylococcus. The first three organisms will frequently grow only under these mephitibic conditions, whereas the others always grow more luxuriantly under them.

Anaerobiosis. Few laboratories have solved the problem of making satisfactory anaerobic cultures. It is extremely important, since many studies have shown that if routine anaerobic cultures could be done, a great many more isolations would be made. Even organisms like the hemolytic streptococcus and pneumococcus are occasionally obligatory anaerobes when first isolated. The inoculation of large (200 by 25 mm.) test tubes filled to at least half their depth with cooked-meat medium usually serves to support the growth of all anaerobic organisms, but isolation in pure culture from such tubes is difficult owing to the abundant growth of other bacteria. For single-colony isolation, no simple method has been devised, and one must use one of several cumbersome methods if anaerobic infection is suspected. The best method, which requires considerably less outlay than the original McIntosh–Fildes or Navy methods, is that devised by Weiss and Spaulding,[8] and Spaulding and Goode,[9] in which a jar is evacuated, filled with carbon dioxide, then re-evacuated and filled with hydrogen, which removes the remaining oxygen in the presence of palladinized asbestos as a catalyst. A chemical method that works fairly satisfactorily is that of Rosenthal,[10] in which chromium is added to sulfuric acid, first liberating hydrogen, and later removing the oxygen by an oxidation of the chromous compound formed.* These methods make possible the inoculation of plates and the isolation of single colonies for identification. Brewer[11] has devised an extremely simple semisolid medium in which all anaerobes tested will grow and which is incubated aerobically. This

*This method has been greatly improved by Mueller and Miller.[12]

method is ideal for ascertaining the sterility of vaccines, toxic filtrates, and serums, but, of course, does not permit the isolation of organisms in pure culture. Its use as an anaerobic blood-culture medium has possibilities still to be explored. Cantor[12] has recently published an ingenious method with which he claims to be able to grow aerobes, mephitibic organisms and anaerobes in the same plate incubated aerobically, and with this he can make single colony isolations.

Staphylococci. Staphylococci are so frequently isolated that it is difficult to assess their significance. The production of yellow pigment, although usually characteristic of virulent staphylococci, is not an adequate criterion of virulence, nor is hemolysis on blood-agar plates. The production of coagulase[13, 14] seems to be quite closely correlated with human virulence, and can easily be tested. A staphylococcal colony or a loop of broth culture is emulsified in 0.5 cc. of citrated human plasma. If this clots within three hours at room temperature, the strain is strongly coagulase positive; if it clots after incubation overnight, it is weakly coagulase positive; and if it remains fluid, the strain is coagulase negative and probably not virulent. Julianelle[15] finds that the fermentation of mannite parallels the coagulase test, but it takes much longer. This test is very useful in determining whether a staphylococcus obtained in a blood culture is a probable invader or a probable contaminant, since most of the former are coagulase positive and the latter coagulase negative.

Streptococci. The proper identification of beta-hemolytic streptococci is extremely important, because infections with these organisms require treatment with sulfanilamide rather than sulfathiazole, and treatment should be continued for a long period to avoid relapses. Unfortunately, many laboratories are unaware of certain peculiarities of these organisms that make their identification difficult. A strain isolated from one of the severest infections seen at the Peter Bent Brigham Hospital was called *Streptococcus viridans* in the laboratory of another institution, because only surface inoculation of blood agar was used. The hemolysin that characterizes beta-hemolytic streptococci is inactivated by oxidation. Consequently, many strains do not produce clear zones of hemolysis on the surface of blood-agar plates, but do so only when pour plates are made and the colonies, growing deep in the agar, are protected from the direct effect of molecular oxygen. For this reason, pour plates containing 5 per cent horse, rabbit or sheep blood in infusion agar should always be made when hemolytic streptococci are suspected, that is, with throat swabs, mastoid swabs and so forth. Dextrose-agar cannot be used, because the presence of dextrose often makes a true beta-hemolytic streptococcus produce green hemolysis. A further reason for making pour plates is that from their appearances beta-hemolytic streptococci of Groups A, B and C[16] can be tentatively identified. Since Group B and Group C infections differ considerably in their course and response to sulfonamide drugs, this identification is of some practical value. If pour plates cannot be made, a simple expedient is to cut under the surface of the agar with the inoculating loop.

Another source of confusion is *Haemophilus haemolyticus*, or so-called "Bacillus X," which produces beta hemolysis both on the surface and in deep pour plates. The use of sheep's blood obviates this difficulty, since it inhibits the growth of this organism.[17] If horse or rabbit blood is used, several hemolytic colonies must always be fished and smeared to make sure that no gram-negative filamentous bacilli are present and that the hemolytic organisms are gram-positive cocci. Mueller and Whitman[18] found that dipping the swab in a dilute solution of disodium phosphate for an hour would get rid of *H. haemolyticus*.

Diphtheria bacilli. The isolation of the diphtheria bacillus from throat cultures has been greatly simplified by the introduction of tellurite-agar plates.[19] On these plates the bacillus forms gray to black colonies. A tellurite-agar plate and Loeffler's slant should be inoculated with each swab. If the former shows suspicious colonies, a stained smear of the Loeffler's slant should be examined, since morphology of the organisms on tellurite agar is atypical. Inspection of the colonies will give an indication of whether the organisms are of the gravis, intermedius or mitis type, the mortality from the disease and the frequency of complications being closely correlated with the type of infection.[20]

Meningococci. Cultures of spinal fluid in cases of meningitis should be made as rapidly as possible and on fresh chocolate-agar slants or plates, since this is the only medium that will grow all the organisms frequently causing meningitis (*H. influenzae* does not grow well on blood agar). At least one plate should be incubated in a candle jar, since increased carbon dioxide tension is necessary for growth of the meningococcus.

Gonococci. The culture of gonococci has been greatly improved and standardized in recent years, through the efforts of a number of workers. A few simple points deserve emphasis. The conditions for successful isolation seem to be the following: suitable mediums, fresh moist plates, slightly increased carbon dioxide tension and a

temperature evenly maintained at 36°C. The method of McLeod et al.,[21] as adapted by Leahy and Carpenter,[22] has become standard in many laboratories. This involves the use of chocolate-agar plates, incubation in a candle jar or similar container at 36°C. for forty-eight hours, and detection of colonies, when they cannot be identified by inspection and smear, by the oxydase reaction, using the dye para-amino-dimethyl-anilinemono-hydrochloride. Other methods have been devised,[23, 24] and one may expect further improvements in the coming years, since chemotherapy has emphasized the importance of cultural methods in ascertaining cures. It seems likely that the use of more than one type of medium may increase the percentage of positive cultures, since certain strains grow poorly on chocolate agar but luxuriantly on 20 per cent blood-dextrose agar. It must be emphasized that the gonococcus is an extremely delicate organism. In taking cultures, all antiseptic agents must be washed away from the genitalia after cleansing, and in females no lubricating jelly, other than plain sterile vaseline, should be used on the speculum, since such jellies contain antiseptics lethal to the organism.[25] Swabs must be planted as soon as possible, or kept in a small amount of ascitic fluid or broth, preferably in the cold until they can be planted. It is possible that the technic mentioned above of allowing the swab to rest on a small amount of blood agar in the bottom of a sterile tube during transportation may be satisfactory.

In differentiating gonococci and meningococci, agglutination tests, as well as agglutinin-absorption tests, are of little or no value because of the presence of cross agglutinins; sugar-fermentation tests in infusion broth containing ascitic fluid, which are controlled by tests set up with known strains, are usually employed.

Stool cultures. Cultures of the stool should be taken whenever possible in cases of acute and chronic diarrheal disease. Despite the marked fall in the incidence of typhoid fever, outbreaks of milder forms of enteric disease remain far too prevalent. These are caused mainly by members of the salmonella (paratyphoid) or dysentery groups. It should be stressed that, whereas in typhoid fever, stool cultures do not become positive until the later stages of the disease, in dysentery, stool cultures may be positive only during the first twenty-four to forty-eight hours. Since sulfaguanidine has been developed for the therapy of these infections,[26] accurate bacteriologic examination of fecal specimens becomes more important. Stool cultures should always be made within an hour or two after passage of the sample, or at least the specimen should be kept cold until delivery to the laboratory. Otherwise, colon bacilli, which always outnumber the pathogens, will overgrow the latter to such an extent that the culture may be reported as negative.

Refinements in the technic involve the use of enrichment methods[27] and of newer mediums to supplant the time-honored eosin-methylene blue agar or Endo's agar plates. For general work, Leifson's[28] mediums — desoxycholate agar and desoxycholate citrate agar — seem to be the most satisfactory, since they permit heavy inoculation and a very clearcut differentiation between lactose-fermenting and nonlactose-fermenting strains.[29] For typhoid work only, Wilson and Blair's[30] bismuth sulfite agar is excellent, and could be used with advantage by all health-department laboratories in following the stools in cases of typhoid fever to see when the patients are ready for discharge.

Blood cultures. Blood cultures properly constitute a large part of the work of every diagnostic laboratory, since a positive blood culture is almost always significant. Contamination of blood cultures is relatively easy, and especial pains should therefore be taken to sterilize the skin thoroughly before venipuncture is performed, and to avoid any contamination with air-borne organisms. Most laboratories take blood cultures by direct inoculation of a flask of broth at the bedside. The citrate method is little more trouble to use and yields a great deal more information. Ten cubic centimeters of blood is removed and inoculated into a vial or flask containing 3 cc. of 2.5 per cent solution of sodium citrate, which prevents clotting. In the laboratory measured amounts (1 and 2 cc.) of blood are pipetted into two Petri dishes, and 10 cc. of dextrose infusion agar is poured into one and 10 cc. of plain infusion agar into the other. The remainder is pipetted into a flask of broth. The advantages of this method are: first, that it enables the laboratory to inoculate the type of medium best suited to the isolation of any particular organism; secondly, that it enables the bacteriologist to count the number of colonies per cubic centimeter of blood, giving a quantitative estimate of the degree of bacteremia; and thirdly, that more rapid identification of the organisms can be made from the type of hemolysis and appearance of the colonies when they grow out on the surface of the agar.

The choice of mediums for blood culture has always aroused considerable dispute.[31] For routine purposes, dextrose infusion broth, dextrose infusion agar and plain infusion agar, the latter included for the identification of the beta-hemolytic

streptococcus, which produces alpha hemolysis in dextrose agar, will be found satisfactory. For isolation of the gonococcus, meningococcus and *Streptobacillus moniliformis*, the addition of 30 per cent ascitic fluid or animal serum is recommended. The isolation of *Brucella abortus* from the blood is often quite difficult,[32] but 2 per cent tryptose broth and agar are recommended by Huddleson et al.[33] Duplicate cultures should be set up aerobically and in a jar with 10 per cent carbon dioxide, which is necessary for the growth of *Br. abortus bovis*. In cases of suspected gas gangrene, puerperal sepsis or undiagnosed sepsis, at least one flask and plate should be incubated anaerobically, since anaerobic organisms invade the blood at times, particularly in these conditions. When gonococcemia, meningococcemia or subacute bacterial endocarditis is suspected, or when previous cultures have been negative in cases of suspected bacteremia, cultures should be incubated under partial tension with a candle jar or with *B. subtilis* cultures in the jar. All routine blood cultures should be held *at least* one week; cultures in suspected cases of subacute bacterial endocarditis, undulant fever, meningococcemia or gonococcemia should be kept three weeks before being discarded as negative.

Cultures from patients receiving sulfonamides. Since the introduction of sulfonamide therapy, the isolation of organisms from the body fluids of patients under treatment with these drugs has often been very difficult. Although such fluids frequently become sterile, cultures may be negative when viable organisms are present because of the marked in vitro bacteriostatic effect of the drug present in the inoculum. The discovery that *p*-aminobenzoic acid would inhibit the action of the sulfonamide drugs in vitro and in vivo[34, 35] has made it possible to overcome this difficulty.[36] Para-aminobenzoic acid can be added to all routine culture mediums in a concentration of about 5 mg. per 100 cc. during their preparation and will withstand autoclaving at a pressure of 15 pounds for twenty minutes.[37] It has been found that if sputum from a patient with pneumonia who has been on chemotherapy is emulsified with an equal amount of a 0.1 per cent solution of *p*-aminobenzoic acid in saline and injected into a mouse, typable pneumococci may be obtained more rapidly and more regularly than when the sputum is injected alone.

Immunologic Procedures

In addition to the direct evidence that the laboratory can supply by the isolation of the causative agent in infectious disease, indirect evidence of the nature of an infection may often be obtained by immunologic tests.

Skin Tests

Skin tests have been used for many years in medicine and are essentially of two types: those that depend on the direct toxic action of the injected material, and those that depend on a hypersensitiveness of the subject to the test substance.

The tests that depend on the toxicity of the test substance are the Schick and Dick tests for the detection of susceptibility to diphtheria and scarlet fever. A measured amount of toxin is injected into the skin. In a susceptible subject the toxin exerts its typical action — the production of an indurated, painful reddened lesion in three days with the Schick test, and of an area of erythema in twenty-four hours with the Dick test. If the subject has a level of circulating antitoxin arbitrarily considered sufficient to protect him from the disease, the injected toxin will be neutralized and no reaction will result. These tests may be misleading, particularly in adults, for in a person previously immunized by injection or contact with the offending organism, there may be little circulating antitoxin, but the cells may possess the ability to elaborate antitoxin very rapidly in response to a slight stimulus. Thus, two weeks after a positive Schick test, a repeat test may be negative, because the test injection has stimulated antitoxin production. Skin tests cannot be used to test for tetanus antitoxin, since tetanus toxin does not affect the skin. The reverse of the Dick test is made use of in the Schultz–Charlton test, in which scarlatinal antitoxin is injected into the skin of a patient with a red rash. If there is blanching at the site in twelve hours, the rash is considered to be scarlatinal.

Most skin tests depend on a state of hypersensitiveness induced by previous contacts with the test substance. This hypersensitiveness tends to assume one of two forms, which perhaps represent different degrees of the same thing, since in certain cases both forms appear at different times. Using Zinsser's[38] classification, one can divide hypersensitiveness into the anaphylactic type, in which circulating antibodies are present and therefore the hypersensitiveness can be transferred by injection of the serum into another person, and the allergic type, in which no humoral antibodies can be found, so that passive transfer is impossible. In the anaphylactic type, the injection of the test substance results in its union with and probable precipitation of the antibodies that exude into the site of injection. Such antigen-antibody complexes are extremely irritating and lead to the local liberation of a substance like histamine. Consequently the typical histamine reaction, a wheal with a zone of erythema about it, appears in about fifteen min-

ules and disappears within an hour or two. In the allergic type of reaction, nothing appears at the site for a number of hours, then induration, pain and redness occur, and in two or three days there is a hard, swollen, tender lesion, which resolves slowly and may even slough at its center. This appears to be due to an inherent sensitivity of the cells themselves, since tuberculin sensitivity has been demonstrated by the cells of a tuberculin-positive guinea pig after they have grown many generations in tissue culture.[39] In both types of reaction, the skin itself must possess the power to react to the irritation, and in moribund patients this often disappears.

A summary of skin tests that are of greatest value in the diagnosis and treatment of disease is given in Table 1.

Foshay[46] has described a sort of reverse Francis test for the early diagnosis of tularemia. Instead of injecting antigen to detect antibodies, he injects antibody to detect antigen. Since the antigen is apt to be circulating early in a disease like tularemia, the injection of specific antiserum is apt to give an immediate reaction. Such tests are seldom necessary and must be carefully controlled with normal serum of the same species. However, Foshay's work is important in emphasizing that skin tests for serum sensitivity must be done with normal serum. Thus, for example, in Type 1 pneumonia, if the rabbit serum to be used in treatment is diluted and injected intradermally, the test is frequently positive, because enough capsular polysaccharide usually circulates to unite with the injected antibody and to give a reaction. If normal rabbit serum is used, this reaction will not occur to confuse the issue.

Serologic Tests

Serologic tests are used in the diagnosis of disease on the assumption that the development of antibodies against a particular infectious agent or some of its products is evidence that the patient has suffered from an infection due to that particular agent. This assumption is based on two premises: that antibodies are specific, and that their formation is always induced by a specific stimulus. These premises have a solid immunologic foundation, because specificity is the most striking characteristic of serologic reactions. But one must be exceedingly cautious in defining specificity. Antibodies have a specific affinity for certain chemical groupings or spatial arrangements, as the work of Landsteiner[50] and many others has shown, but there is nothing to prevent these groupings from occurring in a number of bacteria and viruses. It is this sharing of chemical groupings by dissimilar organisms that gives rise to bizarre phenomena, such as the Weil–Felix reaction, in which the serum of a patient with typhus agglutinates a certain strain of Proteus. As Castaneda[51] has shown, this agglutination is due to the presence of a certain carbohydrate in both the typhus rickettsia and this strain of Proteus. Furthermore, in patients who possess antibody against one antigen, the stimulation of antibody production by another infection may produce a rise in the titer of anti-

TABLE 1. *Clinically Important Skin Tests.*

CONDITION	TEST SUBSTANCE	REMARKS
IMMEDIATE (ANAPHYLACTIC) REACTIONS		
Asthma, hay fever, food allergy, serum sensitivity and so forth	Extracts of pollens, foods, serum and so forth	Some patients skin sensitive without symptoms
Helminth infections (trichiniasis,[40 41] echinococcal disease)	Extract of worms	In trichiniasis delayed reaction first, later replaced (14–20 days) by immediate reaction
Pneumococcal pneumonia (Francis test[42 43])	1:10,000 dilution of capsular polysaccharide of infecting type	Patient must be tested before treatment is begun. If test positive then, cannot be used. If negative, first appearance of positive test after serum administration indicates development of excess of antibody.
DELAYED (ALLERGIC) REACTIONS		
Tuberculosis*	Old tuberculin, P.P.D. (purified protein derivative) better[44]	
Brucellosis*	Brucellergen,[35 48] brucella vaccine	
Tularemia*	Detoxified *Past. tularense* vaccine (Foshay[46])	
Lymphopathia-venerea (lymphogranuloma-inguinale) (Frei test)	Inactivated bubo pus,[47] inactivated infected mouse brain,[45] inactivated infected chick-embryo extract[49]	The last test material is recommended as most satisfactory; all but the first are commercially available.
Chancroid (dmelcos test)	Vaccine (Ducrey's bacillus)	Seldom needed for diagnosis
Pseudoreactions (Dick and Schick tests)	Schick and Dick controls (culture filtrate heated to inactivate toxin)	Due to hypersensitivity to bacterial protein in culture filtrate

*The test remains positive for many years after infection, whether clinical or subclinical. Therefore, its value in diagnosis is in inverse ratio to the frequency of exposure to the infection. Negative tests are valuable in excluding infection.

body against the first antigen as well; this is known as the *anamnestic* reaction.

Since antibodies develop in response to an infection, samples of blood should be drawn early in an infection to serve as a control against later ones. If a single sample of convalescent serum shows antibodies, it means little, but if a sample taken near the onset shows no antibodies, the positive test later means a great deal. To interpret a single serologic test it is necessary to know the frequency of positive tests in the section of the population to which the patient belongs, the titers that can be considered within normal limits and the past history of the patient.

All serologic reactions depend on a union of the antibody in the serum with the antigen for which it has a specific chemical affinity. This union is the fundamental reaction, but it cannot be detected unless secondary reactions take place, which depend on the physical state of the antigen and the conditions of the test.[52] If the antigen is in solution (for example, horse serum) and antibody is added in a test tube, a precipitate will form, if electrolytes are present. If the antigen and antibody unite in the body, anaphylactic reactions occur that give rise to an immediate type of reaction in the skin and to anaphylactic shock in the internal organs. If the antigen is particulate (bacteria or collodion particles coated with a soluble antigen[53]), agglutination will occur when antibody is added in the presence of electrolytes. In the presence of leukocytes, phagocytosis will take place. If complement is present when union of antigen and antibody occurs, it will be fixed by the antigen-antibody complex, and its fixation can be tested by the addition of sensitized sheep cells; such tests must be used when the bacteria will not form satisfactory agglutinating suspensions, as with the gonococcus, or when the antigen cannot be obtained in pure solution, as with virus infections.

The reaction of antigen and antibody has certain peculiarities due to the colloidal nature of antibodies, which account for the zone effects, seen particularly in high-titer serums. Thus, when a patient's serum agglutinates typhoid bacilli to a dilution of 1:2560, there may be very little agglutination below a dilution of 1:80 or 1:160. This is a very strong argument for the use of the test-tube agglutination method with graded dilutions instead of slide agglutination, in addition to the fact that it gives much better quantitative results. Furthermore, the colloidal nature of these reactions requires that they be carried on under relatively constant conditions with regard to pH and concentration of antigen, if results are to be reproducible. Thus, the bacterial suspension used for agglutination reactions must be standardized in some way, the simplest being comparison with turbidity standards of barium sulfate.[54] Test tubes must be thoroughly rinsed after cleaning, since alkalinity from residual soap or acidity from residual cleaning solution will markedly affect the sensitivity of the test. The isoelectric point of most bacteria is in the neighborhood of pH 4.0, and at this point they will flocculate spontaneously, whereas the isoelectric point of the antibodies with which they unite is about 5.6, and at this point agglutination would theoretically be most marked, but not necessarily specific.

Below is given a list of the serologic tests that are of proved value in the diagnosis of disease, with some comments.

PRECIPITATION TESTS

Syphilis (Hinton, Kahn, Kline, Kolmer and Eagle tests). These are very useful, since their ease of performance and high sensitivity make them ideal for the exclusion of syphilis. A comparison of the various tests has been made.[55, 56]

Parasitic Infections. In trichiniasis and echinococcal disease, patients usually develop high titers of precipitins, as well as positive skin tests.[40, 41]

Pneumonia. Test for the presence of capsular polysaccharide in the blood and urine may be a valuable guide to prognosis and thus to therapy.[57]

Spinal Fluid. A ring at the interface between spinal fluid and influenzal or meningococcal antiserum indicates meningitis with the corresponding organism.[2]

AGGLUTINATION TESTS

Brucellosis. Agglutinins when present in titer of 1:80 or more are usually significant. The test is often negative in chronic infections or may be positive in normal subjects in endemic areas, particularly after acute infections.[58]

Tularemia. Agglutinins nearly always rise, usually to high titers, and persist for many years.

Pneumonia. Agglutinins are considered by many to be the most satisfactory method for titrating antibodies.[59]

Dysentery. Agglutinin titer seldom rises high. Occasionally an agglutination test is useful, when positive stool cultures are not obtained. Tests with the Sonne and Shiga types are quite specific; the Flexner group is antigenically heterogeneous.

Salmonella Infections. In this group of infections, agglutination tests are of great value. The work of Kauffmann and White[60] has revealed an extraordinary number of antigens in the group. A properly performed Widal test should include the various organisms that cause enteric fever in the local area. For New England this would be *Eberthella typhosa*, *S. schottmulleri* (paratyphoid B), *S. suipestifer*, *S. enteritidis* and *S. aertrycke*. Two types of agglutination occur: the so-called "H" or flagellar agglutination due to sensitization of the flagellar antigens, and the "O" or somatic agglutination caused by sensitization of the bacterial bodies. H agglutination

is rapid (two hours at 55°C.), and large floccules are formed. O agglutination requires six to twelve hours at 55°C., and fine granular masses are formed. To detect O agglutinins either a nonmotile strain or a specially prepared suspension treated with heat to destroy the H antigen must be used. O agglutinations are very important in doubtful cases, because although a high H agglutinin titer may be produced by prophylactic vaccination or the anamnestic reaction, O agglutinins seldom appear above a titer of 1:80 except in response to infection, when they usually parallel H agglutinins.[61]

Infectious Mononucleosis (heterophil agglutinin test). Serums in this disease agglutinate sheep and ox red blood cells in high titers. This may be associated with a false positive serologic test for syphilis.[62–64]

Rickettsial Infections (Weil–Felix reaction). Patients recovering from rickettsial infections agglutinate certain Proteus strains. Typhus group agglutinates OX_2 and OX_{19}, tsutsugamushi group OX–K, spotted fever group both strains.[65]

COMPLEMENT-FIXATION TESTS

Syphilis (Wassermann test).

Gonococcal Infections. The gonococcal complement-fixation test is much abused. Antibodies appear only infrequently in response to local genito-urinary infections, but do appear in a high percentage of cases of endocarditis and arthritis. The test is useless in following the course of local gonorrhea, but very useful in the differential diagnosis of arthritis and bacterial endocarditis.

Serologic Diagnosis of Diseases Due to Filterable Viruses

Since filterable viruses cannot be grown on ordinary culture mediums and are often isolated with the greatest difficulty by experienced investigators, the diagnosis of these diseases is impossible for the ordinary laboratory. Isolation of the virus is seldom feasible, but the diagnosis of some of these infections by serologic tests is a practicable procedure in well-equipped laboratories, such as those of the Rockefeller Institute, the National Institute of Health or the bacteriology departments of the large medical schools. In virus diseases it is very important to collect serum in the acute stage of the disease and then at the optimum time for the appearance of antibodies, usually three or four weeks after the onset. In many virus diseases, soluble antigens, chemically and immunologically distinct from the virus itself,[66, 67] have been found, and antibodies to these antigens appear in the serums of convalescents usually somewhat earlier than protective antibodies against the virus. These antibodies can be detected by complement fixation, and have been used in the diagnosis of influenza,[68] lymphocytic choriomeningitis,[67] psittacosis[69] and lymphogranuloma inguinale.[70] Antibodies to the virus itself must be detected by their ability to prevent the development of disease in response to a known strain of virus in laboratory animals. Such neutralization or protection tests are widely used in investigative work.

REFERENCES

1. Steinberg, B. Peritoneal exudate: a guide to the diagnosis and prognosis of peritoneal conditions. *J. A. M. A.* **116**:572-578, 1941.
2. Fothergill, L. D. *Hemophilus influenzae* (Pfeiffer bacillus) meningitis and its specific treatment. *New Eng. J. Med.* **216**:587-590, 1937.
3. Alexander, H. E. Type "B" anti-influenzal rabbit serum for therapeutic purposes. *Proc. Soc. Exper. Biol. & Med.* **40**:313, 1939.
4. Davies, J. A. V.: unpublished data.
5. Downie, A. W. Survival of meningococci on swabs and blood agar. *Lancet* **2**:36, 1940.
6. Fothergill, L. D. and Sweet, L. K. Meningitis in infants and children with special reference to age-incidence and bacteriologic diagnosis. *J. Pediat.* **2**:696-710, 1933.
7. Nye, R. N. and Lamb, M. E. Increased carbon dioxide tension as an aid in primary isolation of certain (mephitibic) pathogenic bacteria. *J. A. M. A.* **106**:1075, 1936.
8. Weiss, J. E. and Spaulding, E. H. A simple method for obtaining effective anaerobiosis. *J. Lab. & Clin. Med.* **22**:726-728, 1937.
9. Spaulding, E. H. and Goode, W. G. Anaerobic cultivation as routine bacteriologic procedure in clinical laboratory. *J. Lab. & Clin. Med.* **25**:305-314, 1939.
10. Rosenthal, L. "Chromium-sulphuric acid" method for anaerobic cultures. *J. Bact.* **34**:317-320, 1937.
11. Brewer, J. H. A clear liquid medium for the "aerobic" cultivation of anaerobes. *J. Bact.* **39**:10, 1940.
12. Cantor, A. The maintenance of aerobic, micro-aerophilic, and anaerobic conditions in a petri dish. *J. Bact.* **41**:155-170, 1941.
13. Chapman, G. H., Berens, C., Peters, A. and Curcio, L. Coagulase and hemolysin tests as measures of the pathogenicity of staphylococci. *J. Bact.* **28**:343-363, 1934.
14. Fisher, A. M. The plasma-coagulating properties of Staphylococci. *Bull. Johns Hopkins Hosp.* **59**:393-414, 1936.
15. Julianelle, L. A. Determination of staphylococcal types by fermentation of mannite. *Proc. Soc. Exper. Biol. & Med.* **36**:117-119, 1937.
16. Rantz, L. A. and Jewell, M. L. The relationship of serologic groups A, B, and C of Lancefield to the type of hemolysis produced by Streptococci on poured blood agar plates. *J. Bact.* **40**:1-9, 1940.
17. Krumwiede, E. and Kuttner, A. G. A growth inhibitory substance for the influenza group of organisms in the blood of various animal species. *J. Exper. Med.* **67**:429-441, 1938.
18. Mueller, J. H. and Whitman, L. An improved method for the detection of hemolytic streptococcus carriers. *J. Bact.* **21**:219-223, 1931.
19. Anderson, J. S., Happold, F. C., McLeod, J. W. and Thomson, J. G. On the existence of two forms of diphtheria bacillus — *B. diphtheriae gravis* and *B. diphtheriae mitis* — and a new medium for their differentiation and for the bacteriological diagnosis of diphtheria. *J. Path. & Bact.* **34**:667-681, 1931.
20. Cooper, K. E., Happold, F. C., McLeod, J. W. and Woodcock, H. E. de C. Review of the observations which have accumulated with regard to the significance of diphtheria types in the last four years (1931-1935). *Proc. Roy. Soc. Med.* **29**:1029-1054, 1936.
21. McLeod, J. W., Coates, J. C., Happold, F. C., Priestley, D. P. and Wheatley, B. Cultivation of the gonococcus as a method in the diagnosis of gonorrhea with special reference to the oxydase reaction and to the value of air reinforced in its carbon dioxide content. *J. Path. & Bact.* **39**:221-231, 1934.
22. Leahy, A. D. and Carpenter, C. M. The diagnosis of gonococcal infections by the cultural method. *Am. J. Syph., Gonor. & Ven. Dis.* **20**:347-363, 1936.
23. Cohn, A. and Kruger, R. G. Hemolyzed beef- or sheep-blood media for isolation of the gonococcus. *Am. J. Syph., Gonor. & Ven. Dis.* **24**:295-300, 1940.
24. Pitts, A. C. The laboratory diagnosis of gonococcal infection. *Am. J. Syph., Gonor. & Ven. Dis.* **24**:184-200, 1940.
25. Gillick, F. G., Sulkin, S. E. and Stephens, L. J. A common error in obtaining specimens for the cultural diagnosis of gonococcal infection in women. *Ven. Dis. Inform.* **21**:288-290, 1940.
26. Marshall, E. K., Jr., Bratton, A. C., White, H. J. and Litchfield, J. T., Jr. Sulfanilylguanidine: a chemotherapeutic agent for intestinal infections. *Bull. Johns Hopkins Hosp.* **67**:163-188, 1940.
27. Jones, E. R. The use of brilliant green-eosin agar and sodium tetrathionate broth for the isolation of organisms of the typhoid group. *J. Path. & Bact.* **42**:455-467, 1936.
28. Leifson, E. New culture media based on sodium desoxycholate for the isolation of intestinal pathogens and for the enumeration of colon bacilli in milk and water. *J. Path. & Bact.* **40**:581-599, 1935.
29. Hardy, A. V., Watt, J., De Capito, T. M. and Kolodny, M. H. Studies of acute diarrheal diseases. I. Differential culture media. *Pub. Health Rep.* **54**:287-300, 1939.
30. Wilson, W. J. and Blair, E. M. McV. Use of a glucose bismuth sulphite iron medium for the isolation of *B. typhosus* and *B. proteus*. *J. Hyg.* **26**:374-391, 1927.
31. Penfold, J. B., Goldman, J. and Fairbrother, R. W. Blood-cultures and selection of media. *Lancet* **1**:65-67, 1940.
32. Poston, M. A. Studies on chronic brucellosis. III. Methods used in obtaining cultures. *Pub. Health Rep.* **53**:1-4, 1938.
33. Huddleson, I. F., Hardy, A. V., Debono, J. E. and Giltner, W. *Brucellosis in Man and Animals.* 339 pp. New York: Commonwealth Fund, 1939.

34. Woods, D. D. The relation of *p*-aminobenzoic acid to the mechanism of the action of sulphanilamide. *Brit. J. Exper. Path.* **21:**74-90, 1940.
35. Selbie, F. R. The inhibition of the action of sulphanilamide in mice by *p*-aminobenzoic acid. *Brit. J. Exper. Path.* **21:**90-93, 1940.
36. Strauss, E., Lowell, F. C. and Finland, M. Observations on the inhibition of sulfonamide action by para-aminobenzoic acid. *J. Clin. Investigation* **20:**189-197, 1941.
37. Janeway, C. A. Method for obtaining rapid bacterial growth in cultures from patients under treatment with sulfonamides. *J. A. M. A.* **116:**941, 1941.
38. Zinsser, H., Enders, J. F. and Fothergill, L. D. *Immunity: Principles and application in medicine and public health.* 801 pp. New York: Macmillan Co., 1939. Pp. 340-439.
39. Moen, J. K. Tissue culture studies on bacterial hypersensitivity: persistence *in vitro* of inherent sensitivity to tuberculin of cells from tuberculous animals. *J. Exper. Med.* **64:**943-951, 1936.
40. Spink, W. W. Trichinella antigen: further observations on its use in the diagnosis of trichinosis. *New Eng. J. Med.* **216:**5-8, 1937.
41. Dammin, G. J. Trichinosis: report of a case, with demonstration of the larva in the arterial blood. *New Eng. J. Med.* **224:**357-360, 1941.
42. Francis, T., Jr. The value of the skin test with type-specific capsular polysaccharide in the serum treatment of Type I pneumococcus pneumonia. *J. Exper. Med.* **57:**617-631, 1933.
43. Wood, W. B., Jr. The control of the dosage of antiserum in the treatment of pneumococcal pneumonia. II. The clinical application of the Francis skin test. *J. Clin. Investigation* **19:**105-121, 1940.
44. Long, E. R. and Seibert, F. B. Further studies on purified protein derivatives of tuberculin (P.P.D.): its diagnostic value and keeping qualities in dilution. *Am. Rev. Tuberc.* **35:**281-295, 1937.
45. Evans, A. C., Robinson, F. H. and Baumgartner, L. Studies on chronic brucellosis. IV. Evaluation of diagnostic laboratory tests. *Pub. Health Rep.* **53:**1507-1525, 1938.
46. Foshay, L. Tularemia: a summary of certain aspects of the disease including methods for early diagnosis and the results of serum treatment in 600 patients. *Medicine* **19:**1-83, 1940.
47. Frei, W. Eine neue Hautreaktion bei "Lymphogranuloma inguinale." *Klin. Wchnschr.* **4:**2148, 1925.
48. Grace, A. W. and Suskind, F. H. The use of standardized mouse brain antigen for performance of Frei test for lymphogranuloma inguinale. *J. A. M. A.* **107:**1359-1365, 1936.
49. Grace, A. W., Rake, G. and Shaffer, M. F. A new material (Lygranum) for performance of the Frei test for lymphogranuloma venereum. *Proc. Soc. Exper. Biol. & Med.* **45:**259-263, 1940.
50. Landsteiner, K. *The Specificity of Serological Reactions.* 178 pp. Baltimore: Charles C Thomas, 1936.
51. Castaneda, M. R. The antigenic relationship between *Bacillus proteus* X-19 and *Rickettsiae.* III. A study of the antigenic composition of the extracts of *Bacillus proteus* X-19. *J. Exper. Med.* **62:**289-296, 1935.
52. Mudd, S., Lucké, B., McCutcheon, M. and Strumia, M. On the mechanism of opsonin and bacteriotropin action. VI. Agglutination and tropin action by precipitin sera: characterization of the sensitized surface. *J. Exper. Med.* **52:**313-329, 1930.
53. Cannon, P. R. and Marshall, C. E. An improved serologic method for the determination of the precipitative titers of antisera. *J. Immunol.* **38:**365-376, 1940.
54. McFarland: cited by Zinsser, H. and Bayne-Jones, S. *Textbook of Bacteriology.* Eighth edition. 990 pp. New York: D. Appleton-Century Co., 1939. P. 938.
55. *The Evaluation of Serodiagnostic Tests for Syphilis in the United States.* Supp. No. 1, *Venereal Disease Information.* 49 pp. Washington, D. C., 1935.
56. *The Serodiagnosis of Syphilis.* Supp. No. 9, *Venereal Disease Information.* 224 pp. Washington, D. C., 1939.
57. Bullowa, J. G. M., Bukantz, S. C. and de Gora, P. F. The balance between capsular polysaccharide and antibody in relation to the prognosis and therapy of pneumococcal pneumonia. *Ann. Int. Med.* **14:**1348-1359, 1941.
58. Menefee, E. E., Jr. and Postch, M. A. Significance of standard laboratory procedures in diagnosis of brucellosis. *Am. J. M. Sc.* **197:**646-653, 1939.
59. Finland, M., Brown, J. W. and Rauh, A. E. Treatment of pneumococcic meningitis. *New Eng. J. Med.* **218:**1033-1044, 1938.
60. Kauffmann and White: cited by Topley and Wilson.[61] Pp. 546-550.
61. Topley, W. W. C. and Wilson, G. S. *The Principles of Bacteriology and Immunity.* Second edition. 1645 pp. Baltimore: William Wood & Company, 1936. Pp. 1205-1213.
62. Paul, J. R. and Bunnell, W. W. The presence of heterophile antibodies in infectious mononucleosis. *Am. J. M. Sc.* **183:**90-104, 1932.
63. Davidsohn, I. Test for infectious mononucleosis. *Am. J. Clin. Path. Tech. Supp.* **2:**56-60, 1938.
64. Bernstein, A. False-positive Wassermann reactions in infectious mononucleosis. *Am. J. M. Sc.* **196:**79-83, 1938.
65. Zinsser, H. The rickettsia diseases: varieties, epidemiology, and geographical distribution. *Am. J. Hyg.* **25:**430-463, 1937.
66. Hughes, T. P. A precipitin reaction in yellow fever. *J. Immunol.* **25:**275-294, 1933.
67. Smadel, J. E., Baird, R. D. and Wall, M. J. A soluble antigen of lymphocytic choriomeningitis. I. The separation of the soluble antigen from the virus. *J. Exper. Med.* **70:**53-66, 1939.
68. Hoyle, L. and Fairbrother, R. W. Antigenic structure of influenza viruses; the preparation of elementary body suspensions and the nature of complement-fixing antigen. *J. Hyg.* **37:**512-520, 1937.
69. Meyer, K. F. and Eddie, B. Value of complement fixation test in diagnosis of psittacosis. *J. Infect. Dis.* **65:**225-233, 1939.
70. McKee, C. M., Rake, G. and Shaffer, M. F. Complement fixation test in lymphogranuloma venereum. *Proc. Soc. Exper. Biol. & Med.* **44:**410-413, 1940.
71. Mueller, J. H. and Miller, P. A. A modification of Rosenthal's chromium-sulfuric acid method for anaerobic cultures. *J. Bact.* **41:**301-303, 1941.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 27191

PRESENTATION OF CASE

A sixty-one-year-old Jewish merchant entered the hospital complaining of increasing dyspnea and fatigue.

Two years before admission, the patient noticed the onset of increasing fatigue and shortness of breath, and complained of a feeling of pressure over his left chest. Dyspnea gradually increased in severity and appeared with even the slightest exertion or when he was lying on his back or his left side. Only on his right side could he lie comfortably. On two occasions eight months before admission, while lying in bed, the patient brought up a mouthful of bright-red blood without clots. He did not vomit at the time, nor was he coughing. For several months before entry, while hurrying upstairs, he had experienced a sensation of tightness in his neck, accompanied by a dull ache in the region of the antecubital space of the left arm. These symptoms disappeared immediately with rest. In general the patient had felt well, although he was easily fatigued; his appetite was good and there had been no weight loss.

The patient had had scarlet fever at nine years. His mother, father and one brother had died of heart disease.

On examination the patient was well developed and well nourished and in no apparent distress. The chest was barrel-shaped, with flaring of the costal margins and a suggestion of Harrison's groove. The trachea was shifted to the right, as were the borders of cardiac dullness. There were dullness to percussion and diminished breath sounds and tactile and vocal fremitus over the entire left upper-lung field anteriorly, these same signs being present posteriorly on the left down to the level of the second thoracic spine. The heart sounds were distant, but otherwise normal. One examiner found a blood pressure of 180 systolic, 100 diastolic, in the right arm and 155 systolic, 95 diastolic, in the left; this difference was not recorded by others. The abdomen was normal. Examination of the nervous system was negative except for asymmetry of the face, which was believed to be the result of an old Bell's palsy on the left.

The temperature, pulse and respirations were normal.

Examination of the urine was negative, and kidney-function tests were normal. The blood showed a red-cell count of 4,900,000 with a hemoglobin of 15.1 gm. (photoelectric-cell technic), and a white-cell count of 8500. The nonprotein nitrogen of the blood serum was 24 mg., the protein 6.5 gm. per 100 cc.; a blood Hinton reaction was negative. No tubercle bacilli were found in the sputum on three occasions.

An electrocardiogram showed normal rhythm at 70, with a PR interval of 0.2 second; T_1 was inverted, T_4 was very low and triphasic, and there was slight sagging of ST_2.

An x-ray examination of the chest showed a huge oval mass occupying the anterior aspect of the left side of the chest and extending between the anterior ends of the second and sixth ribs. The mass showed calcification at its margin, moved upward with the ribs at inspiration and displaced the heart to the right. The aorta and heart were otherwise normal, and the diaphragm and visible portions of the lungs were also normal. There was no definite evidence of disease in the ribs, although the anterior ends of the third and fourth ribs were indistinct.

An operation was performed three weeks after admission.

DIFFERENTIAL DIAGNOSIS

DR. FREDERICK T. LORD: May we see the x-ray films?

DR. JAMES R. LINGLEY: The films show this very large mass on the left side of the chest. In the lateral view it lies anteriorly, being flattened against the anterior chest wall. In this film with a little more exposure, one can see a thin rim of calcification around the superior margin. The mass is very smooth and sharply defined, and seems to be slightly lobulated in some areas. The aorta appears normal. The heart is displaced to the right but is not appreciably enlarged. The x-ray appearance is more in favor of tumor than of aneurysm, and the presence of calcification in the wall suggests a benign tumor, especially a cyst.

DR. LORD: The shortness of breath on exertion and on lying on the back or the left side, and the sense of pressure over the left side of the chest, suggest encroachment on the thoracic space, with resulting cardiac disturbance.

The tightness in the neck and the dull ache in the left antecubital space may be ascribed to a disturbance in the circulation in the heart muscle, arising either in consequence of encroachment by the mass or as a result of intrinsic disease of the muscle.

The hemoptysis eight months before admission may have been due to congestion from venous pressure or to erosion of the air passages.

The presence or absence of cough is uncertain, and it is desirable to include a definite statement with respect to this symptom. Although the sputum was examined for tubercle bacilli, its character is not described. A statement regarding the presence or absence of wheezing is also lacking.

That the patient was easily fatigued is interesting, but difficult to interpret. That the appetite was unimpaired and the weight maintained is probably significant.

The flaring of the costal margins and the suggestion of Harrison's groove imply that a tug on the diaphragmatic attachments over a long period led to a bending deformity, and that the intrathoracic mass may have been present for a much longer time than the history indicates.

The complex of physical signs is consistent with the presence of a circumscribed collection of fluid or a solid mass without communication with the bronchi. Failure to mention rales leaves us uncertain about their presence or absence.

The trachea and the heart were displaced somewhat to the right. The blood pressure was slightly elevated. There is a question of difference in the level of the blood pressure in the right and the left arm. The facial asymmetry is not to be regarded as Horner's syndrome.

There are no significant blood findings, with the exception of the negative Hinton reaction, which makes aortic aneurysm unlikely.

The abnormal features of the electrocardiogram may be ascribed to one of three possibilities. They might be due to the administration of digitalis (and we should like to know if the patient had had digitalis), to the slight dextrocardia or to myocardial disturbance. Unless digitalis was administered, I am inclined to think that the electrocardiographic findings are secondary to the encroachment on the intrathoracic space by the mass, but I hope we may have the comments of the cardiologists on this matter.

Since a substernal goiter is a possibility, a basal metabolic rate would be of interest, but is probably of no great importance in the absence of other indications of an overactive thyroid gland. An echinococcus fixation test is desirable in such a problem.

With respect to the source of the mass, without cough or wheezing, an origin in the bronchi or lung is improbable, and the absence of pleural fluid seems to exclude the pleura unless it is an encapsulated pleural process. The mediastinum seems the most likely point of origin, and the location in the left chest was apparently due to least resistance to enlargement in that direction.

With respect to the nature of the mass, an aneurysm is unlikely because of its apparent lack of connection with the aorta in the x-ray films, in addition to the negative Hinton reaction already mentioned.

Various types of tumor are to be considered. A malignant tumor is unlikely, although an originally nonmalignant process may have become malignant. We are therefore left with nonmalignant tumors. The evidence does not warrant a definite diagnosis, and the best I can do is to enumerate the possibilities. Some reliance may be placed on the relative frequency of different types of tumor as a guide in the chance relation, but I appreciate that the chance relation can be upset by Dr. Mallory's assignments.

Neurofibroma is to be considered, but the site of this tumor in the anterior aspect of the thorax makes it unlikely. Lipoma, thymoma, intrathoracic goiter and echinococcus cyst are possibilities. But of all the possibilities, on the basis of the evidence here and the chance relation, I should lean rather more heavily toward a dermoid cyst. If it is a dermoid cyst, it was present at an unusually advanced age. In Hedblom's* series of 191 cases, only one occurred in a patient between sixty-one and seventy years of age. It is to be remembered, too, that about 10 per cent of these cysts become malignant. A positive diagnosis can be made only by finding such elements as hair, squamous epithelium and sebaceous material.

DR. EDWARD D. CHURCHILL: The problem that was uppermost in our minds in dealing with this patient was the question of advisability of operation. The patient was sixty-one years of age; his mother, father and one brother had died of heart disease. He had changes in the electrocardiogram that were interpreted as not due to the tumor, or displacement of the heart. These changes indicated that the patient might be expected during the course of the coming years to develop clinical manifestations of coronary heart disease. Is that putting it fairly, Dr. Bland?

DR. EDWARD F. BLAND: No digitalis had been given?

DR. CHURCHILL: No.

DR. BLAND: I should say so.

DR. CHURCHILL: This prognosis seemed important relative to operation, because this patient could be expected to continue to complain of precordial pressure in the chest referred down his arm and accompanied by increasing dyspnea. In other

*Hedblom, C. A. Intrathoracic dermoid cysts and teratomata with a report of six personal cases and one hundred and eighty-five cases collected from the literature. *J. Thoracic Surg.* 3:22-49, 1933.

words, we were faced for an indeterminable period with a differential diagnosis between intrinsic coronary disease and symptoms due to this tumor. Again, it seemed to me that in a patient who might be expected to develop myocardial insufficiency any factor that could be a burden on the heart, either mechanically or indirectly through limiting vital capacity, should be removed. The patient would then be in a better situation to face his oncoming coronary disease.

We considered, as Dr. Lord did, that this tumor was benign. However, one possibility that we wanted to exclude definitely was putting this elderly patient through an operation for a tumor that might be malignant and had better be treated by x-ray than surgery. For this reason, needle aspiration biopsy was performed. It was really done as part of the operation. A needle was inserted, and a cloudy, brown fluid withdrawn, which under the microscope showed fat and fatty-acid crystals. This finding, of course, gave a definite preoperative diagnosis of dermoid cyst. If I had encountered a solid tumor, I should have tried to secure enough tissue for microscopic diagnosis, and I should have reconsidered the question of radiation therapy if the tumor proved to be malignant sarcoma or teratoma. After having confirmed the diagnosis, however, we went ahead with the operation.

Dr. Lord: I should like to ask Dr. Bland if he thinks he could ascribe the electrocardiographic changes to dextrocardia.

Dr. Bland: No; I am sure you cannot.

Dr. Tracy B. Mallory: Dr. Churchill, do you want to tell us your operative findings?

Dr. Churchill: It was a dermoid cyst. We took it out, and the patient recovered.

Dr. Bland: Do you think it might be of interest to repeat the electrocardiogram, just on the chance that the T waves might have been altered?

Dr. Churchill: Yes; we shall do so.

Clinical Diagnosis

Benign tumor of mediastinum (dermoid cyst ?).

Dr. Lord's Diagnosis

Nonmalignant tumor (dermoid cyst ?).

Anatomical Diagnosis

Dermoid cyst of mediastinum.

Pathological Discussion

Dr. Mallory: Dr. Robert Klopstock studied this cyst with the aid of x-ray films after it had been opened. Most of the calcified material was not an integral part of the wall but merely an adherent precipitate that could be fairly easily scraped off. A few amorphous masses were embedded in the wall, but there was no organization, and no formation of bony trabeculae as in a teratoma.

Dr. Churchill: Dr. Taiana is here from the Argentine. I should like to ask him if that would pass for an echinococcus cyst in the Argentine, where that disease is so prevalent.

Dr. Jiorge A. Taiana: If this lesion with calcification were an echinococcus cyst, it would have to be a dead echinococcus cyst. In cases like this we do not find round masses. Usually we find a cavity, more or less clean, with fluid and with hydatid membrane broken into it. The picture here is completely different.

Dr. George W. Holmes: How much fat was there in the tumor?

Dr. Mallory: Just masses of crystalline fatty acids and cholesterol suspended in the fluid.

A Physician: Was the patient completely relieved?

Dr. Churchill: He said he was, both physically and mentally.

CASE 27192

Presentation of Case

A forty-five-year-old man entered the hospital complaining of exertional dyspnea, cough and weakness.

For the last ten years, the patient had had a morning cough productive of mucoid sputum. Approximately two years before entry, he noticed the onset of shortness of breath on exertion, with a heavy feeling in the chest. His cough grew worse and produced larger quantities of mucoid material, but at no time had it been malodorous or had it contained pus or blood. He consulted his physician, and an x-ray examination of the chest showed bilateral bullous emphysema, with the changes more pronounced on the right, the largest bleb measuring 12 cm. in diameter. He carried on until two months before admission, when the initial symptoms became exaggerated and generalized weakness appeared. An x-ray examination at this time showed the same emphysematous changes, with low diaphragms, but in addition an irregular soft-tissue density in the right paratracheal region, which measured 9 by 8 by 7.5 cm., displaced chiefly the upper lobe and deviated the trachea to the left. Another film nine weeks later demonstrated no change in these findings. The patient stated that during these few weeks before admission he had been given six x-ray treatments, and that coincident with this therapy he had started to vomit, usually in the morning after breakfast and sometimes following

a spasm of coughing. Gradually his generalized weakness increased, and one week before admission a sudden weakness appeared in both legs, which was so severe that he was unable to lift them out of bed. At the time of entry, strength had partially returned in the left leg. During the two months' illness, the patient had suffered from frontal headaches and had lost considerable weight. At twenty he had had gonorrhea, and eight years before admission a right nephrectomy for renal stone. His mother had died from cancer of the uterus.

On examination the patient was pale, weak and cachectic; there was cyanosis and clubbing of the fingers, with an appreciable elevation in the venous pressure. The chest was emphysematous, with slightly less expansion on the right; it was hyperresonant throughout. Scattered rales were heard throughout the chest, most noticeably at the right base. The heart sounds were distant, the blood pressure 108 systolic, 70 diastolic. Abdominal examination was negative except for a right nephrectomy scar. The cranial nerves were normal, but the extremities were wasted and the reflexes on the right side of the body were more active than those on the left. There were ankle clonus and a positive Hoffmann sign on the right; the Babinski signs were normal. Slight but definite motor weakness was present in the right leg and arm (the patient was left-handed), and he performed the heel-to-knee test poorly with his right leg.

The temperature was 101°F., the pulse 100, and the respirations 25.

The urine was normal. The blood showed a red-cell count of 5,080,000 with a hemoglobin of 94 per cent, and a white-cell count of 15,200 with 76 per cent polymorphonuclears. The nonprotein nitrogen of the blood serum was 30 mg. per 100 cc.; a blood Hinton reaction was negative. A lumbar puncture was normal, with a negative spinal-fluid Wassermann reaction. The sputum was negative for tubercle bacilli on one occasion; the stools were normal.

An x-ray film of the chest showed a lobulated mass in the upper anterior mediastinum in close relation to the aorta, but without definite pulsation. No calcification was seen within the mass, and the aorta proximal and distal to it appeared normal. The heart was normal in size and shape. The lungs showed extensive, extremely large, emphysematous bullae, and there was a round 1.5-cm. shadow in the right anterior lower-lung field. Laminagrams showed the mass in the upper mediastinum to be almost exclusively on the right side. It was markedly lobulated, and a separate mass was visible posteriorly in the right tracheobronchial angle. A gastrointestinal series showed displacement of the esophagus to the right and posteriorly by the mass in the upper mediastinum. Otherwise there was no evidence of disease in the upper gastrointestinal tract.

The cough increased. Three weeks after admission, the patient began to suffer from transient episodes of acute dyspnea, which lasted but a few minutes and were associated with clonic contractions of the right leg and twitching of the muscles, with jerking of the entire extremity. Gradually the cough became almost constant, and the sputum thick, tenacious and mucopurulent; and one month after admission the right side of the body was completely paralyzed. Finally, a chest plate showed consolidation in the lower portion of the right lung field consistent with pneumonia, and the sputum yielded a Type 20 pneumococcus. The tumor mass had not changed appreciably so far as could be determined. Death occurred six weeks after admission.

Differential Diagnosis

Dr. Lowrey F. Davenport: We have three separate and somewhat unrelated problems here. The patient had extensive pulmonary emphysema, he had a tumor in his chest, and he apparently died of an intercurrent infection due to the pneumococcus. I think we might take up these three points separately and later see if there is any relation among them.

The background and etiology of pulmonary emphysema are obscure in most cases. Obviously, at the time he came into the hospital, the patient had right-sided heart failure, which is curious because in certain types of extensive emphysema there is no evidence of right-sided heart failure. The emphasis seems to lie in the association of certain emphysematous changes in the lungs to secondary sclerosis in the pulmonary artery. When this pulmonary condition does not occur we get very little change in the mechanics of the right side of the heart. If this were primary pulmonary sclerosis with secondary emphysema, the story would have been entirely different, with a long-standing history of cyanosis, the picture of a "black cardiac," or Ayerza's syndrome, which we often speak of and rarely see. I believe we can exclude a primary pulmonary sclerosis as a cause of the emphysema. At the age of forty-five, it certainly is not senile emphysema. We see considerable emphysema associated with long-standing asthma. That is not the case here. It is interesting that the patient had a cough for ten years. At the time he came in he also had clubbed fingers. If we exclude any primary difficulty with the right side of the heart and with the pulmonary circulation, we have to assume that the clubbed fingers were due to the changes going

on in the lung itself. I do not believe that the cardiac history as given here is sufficient to account for the clubbing of the fingers, nor does emphysema itself cause it. With a ten-year cough, assuming that the patient gradually developed emphysema and later developed right-sided heart failure, it seems to me we have to predicate a long-standing infection. If we try to tie up the extensive emphysema with infection, we can do so only by assuming extensive bronchiectasis involving finer bronchioles, so-called "bronchiolar bronchiectasis." The ordinary suppurative type, with a tremendous amount of infection, very quickly gives clubbed fingers, but is not associated with generalized emphysema. The mass in the chest was discovered almost incidentally. In going through the history, I could find no correlating data with which I could tie up the mass in the chest with the emphysema and the right-sided heart involvement.

May we see the x-ray films at this point?

DR. JAMES R. LINGLEY: The films show an extreme degree of emphysema as described, with large blebs and bullae throughout both lungs, the largest being in the apices, where the appearance simulates a pneumothorax. In addition there is this mass projecting to the right from the upper mediastinum. In the lateral view it extends anteriorly. The laminagraph brings out the margins of the mass a little better. It is sharply defined and lobulated, and the aortic arch appears to be pushed a little to the left side and may be a little dilated in the region of the arch.

DR. DAVENPORT: How intimate was its relation to the aorta?

DR. LINGLEY: Certainly it was in contact with the aorta.

DR. DAVENPORT: We have here an unquestionable tumor in the chest, with very meager definitive data to arrive at the diagnosis. There are several things that may be helpful in trying to untangle the nature of this mass. I think, in general, we believe that a lobulated mass in that region is usually lymphoma, and the obvious signs, which I should interpret as cerebral manifestations, also fit in very well with this diagnosis. However, the lack of response to x-ray therapy is decidedly against it. If it was not lymphoma, what other type of tumor could it have been? I think we must assume that in a man of forty-five the coincidental cerebral symptoms prove it to have been a malignant tumor. On statistical grounds, the diagnosis lies, then, between a cancer and a lymphoma. The shape of the mass is rather against cancer. Bronchiogenic carcinoma should give signs of obstruction. Cancer close to the hilus of the lung, usually does, and only those situated in the periphery, chiefly the adenocarcinomas, would grow to this size without giving clinical and x-ray signs of atelectasis.

The blood findings are somewhat against a cancer that had reached the stage of metastasis. This man came in with a red-cell count of 5,800,000. In our experience, about half the patients with cancer of the lung show a secondary anemia by the time they present themselves for diagnosis. We have to be careful of one thing in this case: the patient may have had a moderate amount of polycythemia on the basis of pulmonary changes and right-sided heart changes, so that for him a hemoglobin of 94 per cent and a red-cell count of 5,000,000 might have represented a drop. Unfortunately, we have no data to support that. In spite of the fact that this tumor did not respond to six lymphoma doses of x-ray therapy, I consider lymphoma the most likely possibility.

There is little to say about the terminal course. The patient had bouts of dyspnea, which do not fit in very well with right-sided heart failure and the changes going on in the lung parenchyma. Perhaps they were cerebral in origin. I think it is also true, if he had metastasis to the brain, that any anoxia of the brain might precipitate convulsions. As a matter of fact, in epilepsy we make use of overbreathing experiments and various types of provoked dyspnea to bring out irritability in the brain.

Having drawn this picture of a man who slowly developed emphysema on the basis of changes in the bronchi and repeated infection, who had what I shall call a malignant lymphoma in the chest and who died of terminal pneumonia and evidence of brain metastases, are there any loopholes in this diagnosis? Is there anything we should go back and try to tie up? He had a nephrectomy eight years prior to admission for renal stone. It does not seem likely that he could have had a hypernephroma at that time that could have been missed.

DR. TRACY B. MALLORY: Are there any suggestions?

DR. EDWARD F. BLAND: I should like to raise some objection to the emphasis placed on right-sided heart failure on the evidence given in this record. It seems to me that the only thing that makes one suspect that the heart might have been involved is that the patient had pulmonary disease of some sort for a long time. The second point is the swelling of the veins in the neck. There are conditions other than right heart failure that give full veins in the neck, for example, mediastinal obstruction. It might have been helpful if something had been said about pulsations in the veins in the neck, because usually there is an absence of pulsations if the swollen veins are the result of mediastinal obstruction in contrast to pul-

sating swollen veins due to back pressure from right-sided heart failure. It is a little unusual to get serious failure of the right side of the heart without some enlargement or dilatation of the heart detectable by physical examination or by x-ray study, and in the films the heart certainly does not look enlarged to me.

Dr. George W. Holmes: I was going to point out the same thing that Dr. Bland has: that the heart is small and there is no evidence of right-sided enlargement.

Dr. Bland: Another point is that the liver was not felt, and I think we must assume that it was not enlarged. No mention is made of edema, and I doubt therefore if right-sided heart failure was an important feature of the illness, even though at postmortem the right ventricle may be found thicker than normal (cor pulmonale).

May I ask Dr. Davenport or Dr. Churchill about this question of pulsating veins in the neck? Is that a reliable differential point between back pressure due to mechanical obstruction as opposed to heart failure?

Dr. Edward D. Churchill: I should have expected a rise in venous pressure with emphysema from the reduced negative intrathoracic pressure.

Dr. Ralph Adams: It seems to me that that lateral view shows atelectasis of a part of the upper lobe, and I should suggest that it is a primary bronchiogenic carcinoma arising in the upper lobe. If that suggestion should prove to be correct, one might explain the signs in the neck by secondary pressure on the vena cava.

Dr. Churchill: How common are intracranial metastases of lymphoma?

Dr. Mallory: They are not at all common, but are not extremely rare.

Dr. Churchill: As a focal lesion?

Dr. Mallory: Viets and Hunter* a few years ago reported five cases of cerebral lymphoma with focal lesions. In leukemia it is commoner to have infiltration without focal signs.

Dr. Churchill: The patient had a little nodule in the lung opposite the one affected. The so-called "primary tumor," in addition to the brain manifestations, speaks very strongly for cancer, it seems to me.

Dr. Holmes: Why do you drop aneurysm without any comment? I am not saying that I think it is an aneurysm, but I wonder how you rule it out so easily.

Dr. Davenport: I think we are forced to rely on you. I assumed, when Dr. Lingley said that the mass was attached to the aorta but was not a part of it, that aneurysm could be excluded. I should not be willing to accept that information from a film not combined with fluoroscopy.

*Viets, H. R. and Hunter, F. T. Lymphoblastomatous involvement of the nervous system. *Arch. Neurol. & Psychiat.* 29:1246-1262, 1933.

Dr. Lingley: The mass is rather lobulated, too.

Dr. Adams: Is it uncommon in the experience of the X-ray Department to see a mass that size in one part of the mediastinum and so little in all the rest?

Dr. Holmes: I should say so.

Clinical Diagnosis

Carcinoma of lung, primary and metastatic.

Dr. Davenport's Diagnoses

Malignant lymphoma of mediastinum and brain.
Pulmonary emphysema.
Right-sided heart failure.

Anatomical Diagnoses

Bronchiogenic carcinoma, with mediastinal and cerebral metastases.
Pulmonary emphysema.
Bronchopneumonia.
Cor pulmonale.

Pathological Discussion

Dr. Mallory: The post-mortem examination showed very extensive emphysema, with large bullae running up to 5 and 10 cm. in diameter. There was a tumor that filled the upper anterior mediastinum and surrounded the great vessels, causing, I am sure, significant venous stasis by mechanical pressure in the thoracic inlet. There was also a tumor in the central portion of the right upper lobe, the appearance of which was characteristic of a primary bronchiogenic carcinoma. It had invaded the pulmonary artery to that lobe, which was nearly occluded by a combination of tumor and secondary thrombus. So far as the rest of the lung was concerned, Dr. Davenport correctly prophesied an extensive terminal bronchopneumonia. There was no marked pulmonary fibrosis, and the appearances were those of idiopathic emphysema, with nothing to give one any lead as to its cause. We did not particularly note bronchiectasis, but I am not prepared to say that it was not there. A bronchiectasis of the smaller radicals is sometimes hard to differentiate from emphysema, and the picture was further obscured by the pneumonic consolidation. The smaller branches of the pulmonary artery showed no sclerotic changes. The right ventricle measured 7 mm., which is quite definite evidence of cor pulmonale, since the heart as a whole was not hypertrophied. A single metastasis, about 2 cm. in diameter, was found in the upper portion of the motor cortex on the left. No metastases were found elsewhere in the body. Microscopically the tumor was a highly undifferentiated carcinoma, probably squamous cell in type.

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The Journal does not hold itself responsible for statements made by any contributor.

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DOCTORS FOR BRITAIN

The American Red Cross has issued an appeal for 1000 American physicians to serve with the British Red Cross in caring for military and civilian war casualties. Volunteers accepted by the British Red Cross will serve either as medical officers with the Royal Army Medical Corps or as physicians with the Emergency Medical Service, a civilian organization under the direction of the Ministry of Health. In addition to the endorsement of the leading professional groups in this country, this appeal has the approval of the Secretary of War, the Surgeon General of the Public Health Service and the President of the United States.

The task of treating civilian casualties, of providing medical care in the large factories and in the expanded navy, army and air corps, and of dealing with the manifold problems incident to wholesale bombing of cities, particularly in preventing epidemics, has proved insurmountable for the medical profession in England. The call for volunteers merits the quick and eager response of American physicians.

The need is urgent, the dangers many, and the rewards almost unlimited. Service with the British Red Cross offers a rare professional experience in the medical technics of modern warfare. Even more important, however, is the opportunity of helping not only soldiers in combat but also those on the other firing line of defense: the population of the ruined cities of the British Isles.

THE FRANCIS AMORY PRIZE

Nearly thirty years ago there died in Beverly an elderly gentleman, Mr. Francis Amory, after a long illness complicated by the miseries of prostatism. His will bequeathed in trust to the American Academy of Arts and Sciences the sum of $25,000, to be allowed to accumulate for twenty-one years, after which the income was to be devoted to a prize to be awarded once in every seven years for the purpose of encouraging and rewarding those engaged in studying, perfecting and publishing methods for the relief of diseases that he described as, "diseases and derangements of the human sexual generative organs in general, and more especially for the cure, prevention or relief of the retention of urine, cystitis, prostatitis and so forth." The testator also suggested that the award may be made to the discoverer of "any notably useful remedy," or to the inventor of "any cunning device or instrument," or if such a person fails to appear, to the writer of "any exceptionally meritorious treatise" on these subjects.

The Academy accepted the trust, and for the first time the income has become available for distribution in the current year. As is so often the case in such bequests, the terms imposed by the testator have been quite difficult to carry out in such a way as to observe their conditions, to do justice to all possible candidates for the prize,

and to promote the public interest. The provision that the work to be recognized must have been done during the seven-year period just preceding the award, and the question whether it is permissible to consider important scientific research the connection of which with the advances described by the testator as the object of his generosity is somewhat remote and indirect, have been the chief perplexities. A committee of the Academy, under the chairmanship of Dr. Roger I. Lee, after long inquiry and deliberation, and with the aid of legal advice when necessary for interpretation of the will, has divided the award among four candidates: Dr. Hugh Young, professor of urology, Johns Hopkins University School of Medicine; Dr. Joseph F. McCarthy, director, Department of Urology, New York Polyclinic Medical School and Hospital; Dr. Carl R. Moore, professor of zoology, University of Chicago; and a European scientist whose name is withheld at present, because he is a citizen of one of the victim states of the Reich, and there is reason to believe that the award would be confiscated or harm be done him by his amiable *Gauleiter*. The accomplishments of Dr. Young, Dr. McCarthy and Dr. Moore that justify the honor to be conferred on them are known to all students of the functions and diseases of the urogenital organs.

The award is to be made at a meeting of the American Academy of Arts and Sciences to be held on the evening of Wednesday, May 14, at 8:15 at 28 Newbury Street, Boston. All interested physicians are invited to attend.

MEDICAL EPONYM

Bundle of His

The original description of this structure, by Wilhelm His, Jr. (b. 1863), is found in the article "Die Thätigkeit des embryonalen Herzens und deren Bedeutung für die Lehre von der Herzbewegung beim Erwachsenen [The Activity of the Embryonal Heart and Its Significance in the Theory of the Contraction of the Adult Heart]," which appeared in *Arbeiten aus der medizinische Klinik zu Leipzig* (14–49, 1893). A portion of the translation follows:

> After prolonged investigation, I have succeeded in finding a muscular bundle that connects the auricular and the ventricular septums. This has hitherto escaped observation because, on account of its small dimensions, it is visible in its entire extent only if this area is cut lengthwise. Up to the present time, I have been able to trace the course of the bundle in such sections and also in serial sections in a grown mouse, a newborn dog, two newborn infants and one adult (thirty years) human being. The bundle arises from the posterior wall of the right auricle near the auricular septum in the atrioventricular groove, continues along the upper margin of the ventricular septum with frequent interlacing of the muscle fibers of the two structures, and then runs forward until, near the aorta, it forks, dividing into a right and left branch. . . .
>
> R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

ANNUAL MEETING OF THE COUNCIL

The annual meeting of the Council will be held in the Swiss Room of The Copley-Plaza, Boston, on Wednesday, May 21, 1941, at 10:30 o'clock.

Business:

1. Presentation of record of special meeting held April 9, 1941, as published in the *New England Journal of Medicine* for May 8, 1941.
2. Nominating Committee retires to deliberate.
3. Reports of standing and special committees.
4. Election of officers and orator.
5. Appointment of committees for ensuing year, both standing and special.
6. Incidental business.

Robert N. Nye, *Secretary* pro tempore.

SECTION OF OBSTETRICS AND GYNECOLOGY*

Raymond S. Titus, M.D., *Secretary*
330 Dartmouth Street
Boston

Death Associated with Infection and Stillbirth

A thirty-five-year-old multipara arrived at the hospital in active labor at term with a temperature of 103.6°F. She had never been examined during this pregnancy, and had had no prenatal

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

care whatsoever. The past history was essentially noncontributory. The patient had three living children, but more specific information concerning the labor and delivery in these pregnancies was not obtained. There was no history of previous medical complications.

Physical examination on entrance was essentially negative. There was no evidence of anything abnormal in the lungs; no mention was made of the throat. The heart was rapid, with a rate of 120, but there was no mention of a complicating disease. The uterus was enlarged to a size consistent with full-term pregnancy, the membranes had ruptured, apparently shortly before admission, and the patient was in active labor. After ten hours and forty minutes, the patient was delivered normally of a stillborn child. Death occurred twenty hours after delivery.

Comment. This is a most unusual story. There was nothing in the history to explain the infection that must have been present, and unfortunately, permission for an autopsy was not obtained. In the absence of evidence of pneumonia, — which, if present, would undoubtedly have been recognized, — it seems likely that the patient was suffering from a generalized infection, possibly streptococcal in origin. Obviously, cultures of the blood and lochia should have been made.

The stillbirth was probably due to the fever, but early intrauterine sepsis is a possibility. Since this maternal death occurred in 1937, before the advent of chemotherapy, one cannot judge what the outcome would have been if the patient had been treated with one of the sulfonamides.

APPLICANT FOR FELLOWSHIP

Owing to an error, the following name was omitted from the list of applicants for fellowship printed in the April 10 issue of the *Journal*.

PLYMOUTH DISTRICT

Bernard H. Beuthner, 24 School Street, Middleboro.
University of Breslau, 1925.

Ralph C. McLeod, *Secretary*.

DEATHS

HOLT — CHARLES H. HOLT, M.D., of Pawtucket, Rhode Island, died April 26. He was in his sixty-first year.

Born in Bradford, England, Dr. Holt attended Brown University and received his degree from the Harvard Medical School in 1906. He was president of the Rhode Island Medical Society, and was a fellow of the American Medical Association and a former member of the Massachusetts Medical Society.

His widow, two sisters and a son survive him.

WELLES — DELBERT A. WELLES, M.D., of Fitchburg, died May 1. He was in his seventy-eighth year.

Born in Concord, New Hampshire, he attended Thetford Academy, Vermont, and received his degree from George Washington University School of Medicine in 1898. He trained in government hospitals for six years before going to Fitchburg. He had been a city councilor since 1939.

He was a fellow of the Massachusetts Medical Society and the American Medical Association.

MISCELLANY

NOTES

On May 5, Dr. Walter B. Cannon, George Higginson Professor of Physiology, Harvard Medical School, was presented the Friedenwald Medal of the National Gastroenterological Association. This was the first award of the medal, and the accompanying citation read, "In recognition of his pioneer utilization of the x-rays in gastroenterology, and his important contributions to the mechanics of digestion, to the elucidation of the sensations of hunger and thirst, and to the development of the science and practice of gastroenterology."

The two awards of $100 each offered by the Laymen's League Against Epilepsy in 1940 for the best original unpublished observations or investigations bearing on the subject of epilepsy have been granted as follows: for work done in a state epileptic colony or mental hospital, to Dr. Walter L. Bruetsch, Central State Hospital, Indianapolis, Indiana, "Rheumatic Epilepsy"; for work done elsewhere, to Dr. Frederick A. Fender, Stanford University Hospital, San Francisco, "Convulsions Following Remote Electrical Stimulation of Subcortical Cerebral Levels."

At a meeting of the Trustees of Middlesex University, held on April 12, the following new trustees were appointed: Stanley R. Latshaw, Haddam, Connecticut; Alton L. Miller, Brookline; Joseph F. O'Connell, Boston; Charles J. O'Malley, Boston; and Samuel H. Wragg, Needham Heights, Massachusetts.

CORRESPONDENCE

"TEN-DAY PAPER" FOR ADMISSION TO STATE MENTAL HOSPITALS

To the Editor: It seems advisable to call to the attention of the medical profession the basic provision and intent of Section 79, Chapter 123, General Laws, which is the authorizing statute for a temporary-care, so-called "ten-day paper," admission of a patient to a mental hospital within this commonwealth.

This statute provides in part that the superintendent of a hospital for the insane may, upon request of certain designated persons, receive as a patient for a period not exceeding ten days a person who is "in need of immediate care and treatment because of mental derangement other than drunkenness."

There appears to be a general impression that this type of admission is primarily a *ten-day observation*. Scrutiny of the statute does not support this view. It is intended to provide an *emergency admission* for the patient who must be hospitalized immediately, and who should not await usual commitment proceedings before admission for reasons of his own personal welfare or the safety of the public.

Other sections of Chapter 123 provide for observation in a mental hospital. Section 77 authorizes the usual thirty-day observation; Section 100 includes observation for those under complaint or indictment; Sections 103 and 104 allow observation for those under sentence for crime.

It is therefore recommended that the use of the "ten-day paper" be restricted to those cases in which the patient is "in need of immediate care and treatment because of mental derangement other than drunkenness."

CLIFTON T. PERKINS, M.D., *Commissioner*
Department of Mental Health

100 Nashua Street
Boston

MEDICAL OFFICER WANTED FOR THE SCHOOLSHIP *NANTUCKET*

To the Editor: The Massachusetts Nautical School is desirous of securing the services of a medical officer for the Schoolship *Nantucket* for the summer cruise of 1941, the itinerary of which covers 8245 miles, ending in Boston on September 9.

The medical officer of the *Nantucket* will have charge of safeguarding the health of 85 cadets, and of the officers and crew, numbering about 30. It is important to have a man not only of good professional ability but of the highest character.

W. K. QUEEN, *Chairman*

100 Nashua Street
Boston

REPORTS OF MEETINGS

BOSTON ORTHOPEDIC CLUB

There was a regular meeting of the Boston Orthopedic Club at the Boston Medical Library on January 20, with Dr. Augustus Thorndike, Jr., presiding.

The first paper was by Dr. A. B. Ferguson and was entitled "Wedging Round Back of Adolescence." This condition has been described under various titles, including "vertebral epiphysitis" and "Schuermann's disease." It is characterized by gradual development of anterior wedging of one or more of the dorsal vertebral bodies during adolescence and is a common condition. The patient with a wedging round back has poor posture, with round shoulders and exaggeration of the posterior curve of the dorsal spine; the anterior cervical and lumbar curves are increased, and the abdomen may be protuberant. Fatigue is the commonest symptom before and during adolescence, but later rigidity of the spine may reduce fatigue. Pain is not common in those who are quite young but is frequent at and after the age of seventeen, when osteoarthritic changes may be evident.

In a group of these cases studied for possible etiologic factors it was found that the condition was not confined to a particular type of person; that debilitating disease may favor its development; that the frequency of such conditions as coxa plana and Osgood–Schlatter's disease was not sufficient to suggest an etiologic relation; and that familial tendencies may favor its development, although, obviously, the condition is not wholly congenital. Dorsal round back may be noted clinically, but the diagnosis of wedging round back of adolescence is usually a roentgenographic problem because it is necessary to rule out by roentgen examination certain other causes of round back or kyphosis, such as fracture, hemivertebra, incomplete segmentation, malacia, chondrodysplasia, rheumatoid arthritis and specific infectious diseases. The features of this condition are progressive multiple anterior rounded wedging of the dorsal vertebral bodies. The wedging may progress indefinitely, but there is rarely much increase after the age of twenty. During adolescence, irregularity of the intervertebral disks and apophyseal plates may be evident, and at or after the age of seventeen osteoarthritic calcareous lipping may be present. The vertebral bodies do not become ankylosed, nor do they present areas of destruction or abscess formation.

Since immobilization in plaster has failed to prevent the progress of the deformity and the presence of pain, weakness and fatigue, it was considered likely that inflammation, which should be benefited by such a regimen, is not the etiologic factor in wedging round back of adolescence. From a consideration of the development of the vertebral column and a review of the progress of cases in which x-ray films taken before adolescence were available, Dr. Ferguson concluded that in certain persons a persistence of a vascular area at the middle of the vertebrae anteriorly weakens the structure and results in compression where the stress is greatest — in the dorsal region. It was emphasized that the wedging occurs by compression at the middle of the anterior surface of the body, not by compression of the upper or lower surfaces. The apophyseal plates appear later roentgenographically, and the irregularity found in this condition was considered a secondary phenomenon resulting, like the later osteoarthritic lipping, from impaired nutrition. In this conception, there is no need to assume the presence of disease in the vertebral body or elsewhere. It is simply that all people do not have spines entirely suited to the erect posture.

The treatment indicated for the prevention of deformity, fatigue and pain should be reduction of stress on the front portion of the vertebral bodies in the dorsal area. This treatment can be very simply accomplished by means of a postural brace, a modification of an ordinary short spinal brace. The usual horizontal bars at the buttocks and vertical bars along the spine are retained, but at the upper extremity of the vertical bars a padded metal block is placed. The height of the brace is such that the pad impinges on the back immediately below the area of the round-back deformity. The brace does not itself support the dorsal spine, but maintains a lumbar posture that excites active extension of the dorsal spine. The brace is not effective for older patients, when the spine is not flexible, the adolescent period of rapid growth having been passed.

Treatment of wedging round back of adolescence at the New York Orthopedic Hospital has been mainly along conservative lines. Nearly all the patients had exercises to strengthen muscles and keep the spine mobile. In a few cases, a short spine brace, such as that described above, was used, and in others the spine was fused surgically in the deformed area, with or without an attempt to correct the deformity. Treatment by exercises did not prevent increase of deformity or the development of ache or fatigue. The results of surgical fusions were not, on the whole, an improvement over the results obtained by exercises. Fusion of the area of greatest deformity did not prevent progress or maintain correction of the deformity except in a few cases, nor was there a demonstrable favorable effect on the tendency to increasing pain and fatigue with advancing age. Nevertheless, some patients with distressing fatigue and pain were much better after spine fusion, and such treatment may be es-

sential in such cases. As a rule, if deformity did not increase in the fused area, it did increase in the areas adjacent to the fusion, and it seems that one could not expect to prevent increase of deformity in the adolescent unless the entire dorsal spine were fused; however, there seems to be no justification for extensive surgery in the treatment of such a mild condition. Use of the brace definitely tended to inhibit the progress of deformity and the development of symptoms in adolescent and preadolescent patients. When ache or fatigue is marked the patient is apt to be too old to derive benefit from the brace. If the spine has become too stiff to straighten definitely when the brace is applied, it is too late to derive benefit from the brace. Wedging round back of adolescence should be diagnosed in the preadolescent years, when the simple treatment by postural brace may prevent the development of troublesome deformity.

During the discussion, Dr. John J. Kuhns suggested that the roentgenographic appearance of a persistent vascular canal may be an artefact. In 1000 autopsies at the Children's Hospital, with many clinical diagnoses of wedging round back, no pathologic changes were found. Furthermore, not all adults with a persistent canal have evidence of past or present wedging round back. Treatment should be carried out early, but Dr. Kuhns finds that many patients need elaborate jackets rather than simple back braces, which probably are effective only where there is a well-developed postural reflex.

Dr. Joseph Barr, of the Massachusetts General Hospital, agreed that there was an interference of epiphyseal growth rather than an epiphysitis. He believes that the presence of tight lower extremities may cause an increased lumbar lordosis and a functional kyphosis. As for treatment, it is found that exercises help materially even when roentgenographic evidence does not confirm the improvement.

In answer, Dr. Ferguson replied that the x-ray evidence undoubtedly is not artefact. He suggested that those patients with roentgenographic evidence but no clinical disease have minimal vascular impairment or good musculature and posture, whereas persistence of the vascular canal in the lumbar region causes no symptoms because of the absence of stress. In regard to the hip flexion mentioned by Dr. Barr, it was stated that this is usually present in the older patients, and therefore is more probably a secondary phenomenon.

The second paper, "A Recently Defined Destructive Lesion of Bone," was presented from the clinical aspect by Dr. William T. Green and from the pathological by Dr. Sidney Farber. The authors reported the occurrence of destructive lesions in the bones of 10 children, all under twelve years of age, studied at the Children's Hospital during the last ten years. The disease process was limited almost completely to the destructive lesions in the skeletal system. These lesions were either single or multiple and involved mainly the flat bones, particularly the skull, ribs and pelvis. They were seen in many other bones, but never at the distal ends of extremities. When single, the lesions had the roentgenographic characteristics of solitary bone cysts. The multiple lesions could be compared most accurately in distribution and punched-out appearance with either myeloma or metastatic cancer. More than twenty-six areas of involvement of the skeleton were noted in one patient. The presenting sign was usually swelling or pain. Swelling was more prominent than pain when the skull was involved. Healing occurred readily under roentgen-ray therapy. Nine of the 10 patients were apparently well when examined recently. One patient died outside the hospital; the details cannot be obtained.

Biopsy specimens were obtained from all the lesions. The microscopic picture varied considerably, but in general it was essentially a granulomatous process in which eosinophilic infiltration was frequently a prominent feature. Activity of the marrow cells in the involved areas was evident in several cases to such an extent that a picture characteristic of myelocytic myeloma was suggested by the initial studies. Various gradations from the purely granulomatous reaction to a definite xanthomatous process could be demonstrated in various sections examined. Small to large amounts of lipids, stainable by the Scharlach R method, were present in the lesion.

The lesion clinically and microscopically conforms to a picture recently described under the name "solitary granuloma of bone" or "eosinophilic granuloma of bone." A comparison of the pathologic material obtained from these 10 patients with the bone and visceral lesions found in Schüller–Christian's disease and with pathologic specimens from the lungs, lymph nodes and skin of a condition that has come to be known in recent years as Letterer–Siewe's disease has led to the conclusion that all three conditions represent variations of the same basic disease process. Preliminary bacteriologic and animal-inoculation studies have thus far been negative in the group under discussion, as well as in Schüller–Christian's disease and Letterer–Siewe's variation of that disease. Further studies of the etiologic basis for the benign destructive lesion under discussion, as well as of the other variants of the Schüller–Christian syndrome, are under way. There appears to be no justification, on the basis of this experience, for considering eosinophilic or solitary granuloma of bone as either a new or a separate disease entity.

HARVARD MEDICAL SOCIETY

A regular meeting of the Harvard Medical Society was held at the Peter Bent Brigham Hospital on January 28, with Dr. Elliott C. Cutler presiding.

The first case was that of a sixty-nine-year-old man who entered the hospital because of intense jaundice and itching. For four months he had noticed weight loss and increasing lassitude and fatigue. Three weeks before admission he had been troubled with constipation and crampy right lower-quadrant pain. Anorexia had been present for two weeks, jaundice for five days and nausea for one day. There was no previous history of right upper-quadrant pain or other gall-bladder complaints. Physical examination revealed a chronically ill, emaciated, jaundiced man in no distress. The abdomen was tender in the right upper quadrant; the liver edge could be palpated 2 cm. below the right costal margin, and was round, firm and nontender. Laboratory data revealed normal red-cell and white-cell counts, a +++ test for bile in the urine, an icteric index that rose from 50 to over 100, a blood diastase positive at 1:68 and normal plasma-protein levels and liver function tests. Roentgenograms demonstrated an extrinsic mass deforming the duodenum. The probable diagnosis of pancreatic neoplasm was made, but Dr. Merrill C. Sosman stated that such a diagnosis could not be made from x-ray studies alone, for tumors cannot be seen until they are very large, and may well be cysts instead of neoplasm.

The second case was that of a sixty-nine-year-old man who entered the hospital because of anorexia of one month's duration. His stools had become increasingly lighter and his urine darker, and two weeks before admission his friends had noticed that he was jaundiced. He had had some vague chest pains, which radiated to

his right side, and there had been an indefinite weight loss. Physical examination revealed a well-developed, obese and jaundiced elderly man. There was an apical systolic murmur without any cardiac enlargement. The abdomen was large, and without any tenderness or masses. The liver descended 3 cm. below the costal margin, and its edge was smooth and firm. There was a direct inguinal hernia on the left side. The icteric index was 60, and the bleeding and clotting time normal. X-ray study was negative. The patient was operated on, and a cholecystogastrostomy carried out, with subsequent decrease of symptoms of jaundice, improvement in the color of the stools and urine, and a drop in the icteric index to 30. Dr. Sosman stated that here again no preoperative diagnosis was possible, but that postoperatively by roentgenograms there was no increase of the gallbladder indenture and no regurgitation of barium into the gall bladder. Dr. Cutler pointed out that the usual type of anastomosis may allow infection to ascend into the liver, and this has led to the valvular type of anastomosis employed by Dr. Zollinger. In this patient, the wound had been anesthetized to allow full and painless respiration immediately after operation.

The paper of the evening was "Carcinoma of the Pancreas," delivered by Dr. Frank Glenn, of Cornell University Medical College. As an introduction the speaker pointed out that this disease annually causes almost as many deaths as pulmonary cancer. Pathologically, cancer usually appears in the head (70 per cent), its association with biliary disease is not constant, and the nodules may be diffuse or scattered. Metastases to regional lymph nodes are found in 90 per cent of cases, to the liver in over 50 per cent; there are peritoneal implants in less than half the cases, and skeletal spread is noticed in 20 or 30 per cent. Microscopically there may be a cylindrical adenocarcinoma from the duct system that tends to be cystic, a tumor with large granular cells similar to those of the alveoli, or an islet-cell carcinoma.

The incidence of the condition was found to be 1 in 752 hospital admissions. The chief complaint was pain in 68 per cent of patients, jaundice in 50 per cent and occasionally other symptoms. The high incidence of pain was emphasized, and it was noted that there is apt to be more itching from this type of jaundice than from that of a common-duct stone. The leading symptom was loss of weight (97 per cent). On physical examination jaundice was found in 68, hepatomegaly in 53, abdominal tenderness in 37 and a palpable gall bladder in only 34 per cent of the cases. In regard to laboratory findings, blood counts were found to be variable, stools were found to contain blood in over half the cases, but no other data were considered significant. The importance of guaiac-positive stools as evidence of intestinal invasion was suggested. Roentgenograms were carried out in the majority of cases and were reported negative in 50 per cent. Of the remaining half, defects were noted in the pylorus and all portions of the duodenum, with diagnosis of probable carcinoma of the stomach, duodenal ulcer and carcinoma of the head of the pancreas in equal numbers. The duration of life after the onset of signs and symptoms was found to average only slightly over nine months.

Treatment was variable and discouraging. Palliative operations apparently relieved the biliary obstruction, decreased the itching and increased the appetite. The occurrence of cholangitis was discouragingly frequent, the mortality was high, and the duration of life was not increased. Curative operations, which attempt to extirpate the tumor, have been found technically difficult, and there is the added disadvantage that the patients do poorly postoperatively, probably owing to the inadequacy of attempted substitutes for the external pancreatic secretions. Dr. Glenn considers the external secretions important for maintaining proper pancreatic and hepatic functions, for ligations of the ducts in dogs lead to fibrosis and decrease of active pancreatic tissue and an early and marked increase in the liver fat. He proposes to preserve the secretions by transplanting the duct-containing pancreas to the posterior stomach wall. In animals, the pancreas has been found grossly and microscopically normal while the patency of the ducts is maintained and the liver remains normal. Dr. Glenn therefore advocated removal of the tumor-bearing area and transplantation of the remaining ducts to the posterior stomach wall. Of 3 possible cases operated on, 2 of the patients have shown too much induration around the head of the pancreas at the second stage, whereas the third was found to have cancer at the ampulla of Vater. It was therefore suggested that one-stage operations might be advisable. One important feature of this type of operation is the impossibility of any ascending infection.

In conclusion, Dr. Glenn suggested that the hope for the future lies in earlier diagnosis and in improved and more radical surgery. The important clues for earlier diagnosis are abdominal pain, loss of weight and jaundice without any other definite cause. Improvement in treatment should include earlier and more frequent exploratory operations.

The discussion was opened by Dr. David Cheever, who pointed out that the pancreas should be considered in both the acute (pancreatitis) and the chronic (carcinoma of the head of the pancreas) surgical abdomen. He has found in the latter condition that although pain is common, it is not similar to that of biliary colic. Instead, it is usually vague and persistent, and radiates toward the back or left flank. Roentgenographic studies are of questionable value, even when the tumor is in the head, and entirely miss those in other parts of the gland. Cases have usually seemed inoperable, owing to seeding of the peritoneum, especially in the right upper quadrant. Dr. Cheever believes that cholecystogastrostomy offers the most favorable prognosis at present, for it usually affords a year and a half of fairly comfortable existence, often followed by sudden death.

Dr. S. J. Thannhauser stated that diagnosis can be facilitated by the use of the double-barrel duodenal tube and the secretin test. He is of the opinion that the findings of 80 to 90 milliequiv. of alkali per liter following secretin is significant. He has found that pain below the left costal margin may simulate that of cardiac origin. He stated that in his opinion choline is not related to the fatty metabolism of the liver in man. He has had no good results with the feeding of raw pancreas.

Dr. J. E. Dunphy has also found the incidence of pain to be about 68 per cent, but he differentiates the site of the lesion by the character and site of the pain: Obstruction of the ducts by a small tumor is apt to produce colicky pain, which diminishes as the disease progresses; in other cases, there is an ache in the back, with vague abdominal pain, which is worse at night and when the patient is recumbent; large tumors of the body of the pancreas may affect the celiac plexus and cause excruciating pain, which may radiate even to the chest.

Dr. Sosman stressed the importance of diagnosis by exclusion, for loss of weight in 97 per cent of cases indicates that failure to lose weight can fairly well rule out

this condition. The possibility of relieving pain by irradiation in inoperable cases was advanced.

The meeting was closed by Dr. Glenn, who suggested that not only the alkalinity but also the volume following the use of secretin is significant. He has found irradiation therapy inefficacious in allaying pain. He has observed glycosuria intermittently in 14 per cent of his preoperative patients, whereas Opie has found evidence of true diabetes in 10 per cent of such cases at autopsy.

NOTICES

FRANCIS AMORY AWARDS

Members of the medical profession are invited to attend a meeting at the American Academy of Arts and Sciences, 28 Newbury Street, Boston, on May 14, at 8:15 p.m., for the occasion of the presentation of the Francis Amory Awards to three investigators for their notable contributions to the treatment and cure of diseases and derangements of the genitourinary organs.

The investigators are Dr. Joseph F. McCarthy, professor of urology and director of the Department of Urology, New York Polyclinic Medical School and Hospital; Dr. Carl R. Moore, professor of zoology, University of Chicago; and Dr. Hugh H. Young, professor of urology, Johns Hopkins University School of Medicine.

Each recipient will briefly describe his investigations, placing special emphasis on the circumstances leading to the culmination of the work for which the prize is given.

TRUDEAU SOCIETY OF BOSTON

The annual meeting of the Trudeau Society of Boston will be held at the Belmont Hospital, Worcester, Massachusetts, on Thursday, May 15, at 4 p.m.

PROGRAM

Pulmonary Tuberculosis and Pregnancy. Dr. Arthur D. Ward.

Discussion by Drs. Samuel C. Gwynne, Francis D. Hart and Frederick L. Good.

Carcinoma of Lung and Tuberculosis. Dr. Marguerite D. Shepard.

Discussion by Drs. Ernest L. Hunt and Ralph H. Adams.

Rectal Fistula in the Tuberculous. Dr. Percy A. Brooke.

Discussion by Dr. Andrew Taylor, of Hartford, Connecticut.

Treatment of Guinea Pig Tuberculosis with a New Chemical Compound. Drs. Raymond H. Goodale and Leslie A. MacClintock.

Gomenol Therapy in Pulmonary Tuberculosis: Presentation of cases. Dr. Robert H. Baker.

Discussion by Drs. Donald King and Nahum R. Pillsbury.

SOUTH END MEDICAL CLUB

The next regular meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, May 20, at 12 m. Dr. Henry Jackson, Jr., will speak on "Certain Practical Aspects of Blood Disorders as Seen by the General Practitioner."

Physicians are cordially invited to attend.

BOSTON DISPENSARY

There will be a clinical staff meeting of the Boston Dispensary in the Pratt Hospital Auditorium on Friday, May 16, at 12:30 p.m. Dr. Burrill B. Crohn, chief, Gastrointestinal Service, and associate in medicine, Mt. Sinai Hospital, New York City, will speak on "Sprue versus Ileojejunitis." Luncheon will be served at 12 m.

All interested members of the profession are cordially invited to attend.

1941 GRADUATE FORTNIGHT

The 1941 Graduate Fortnight of the New York Academy of Medicine will be held from October 13 to 24. The purpose of this meeting is to make a complete study and authoritative presentation of a subject of outstanding importance in the practice of medicine and surgery. The current topic is "Cardiovascular Diseases, including Hypertension."

There will be a carefully integrated program that will include morning panel discussions, afternoon clinics and clinical demonstrations at hospitals of New York City, evening addresses and a scientific exhibit. The evening sessions at the Academy will be addressed by recognized authorities from leading medical centers of the United States and Canada. The comprehensive exhibit will include books and roentgenograms, pathological and research material, and demonstrations of clinical, laboratory and therapeutic methods.

The following subjects will be included: basic hemodynamic principles essential to the interpretation of cardiovascular disorders; heart failure; diagnosis and treatment of coronary insufficiency; pathology of arteriosclerosis, with special reference to coronary arteries; observations on social significance and recent advances in the treatment of arteriosclerosis; advances in the knowledge of endocarditis, with special reference to the therapy of subacute bacterial endocarditis; neurocirculatory asthenia and related problems in military medicine; syphilis of the cardiovascular system; arrhythmias, including paroxysmal tachycardia and their treatment; the value and limitations of the electrocardiogram in medical practice; evaluation of drugs used in the treatment of cardiovascular diseases; surgery of the heart and large vessels; surgical treatment of peripheral embolism and peripheral aneurysm; thrombophlebitis; the use of heparin; Raynaud's disease; thromboangiitis obliterans; experimental studies related to shock; influence of extrinsic factors on the coronary flow and the clinical course of heart disease; treatment of heart disease in childhood; management of heart disease in pregnancy; mechanism of essential hypertension; mechanism and treatment of pulmonary edema; rheumatic heart disease; and effects of renal extracts of hypertension.

The Academy provides this program for the fundamental purpose of postgraduate medical education; consequently all members of the medical profession are eligible for registration. A complete program and registration blank may be secured by addressing: Dr. Mahlon Ashford, New York Academy of Medicine, 2 East 103d Street, New York City.

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Sunday, May 11

Monday, May 12

American Association for the Study of Goiter. Hotel Statler, Boston.

12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

Tuesday, May 13

American Association for the Study of Goiter. Hotel Statler, Boston.

*9–10 a.m. Subacute Bacterial Endocarditis with Special Reference to Treatment. Dr. J. M. Faulkner. Joseph H. Pratt Diagnostic Hospital.

12:15–1:15 p.m. Clinicoroentgenologic conference. Peter Bent Brigham Hospital amphitheater.

Wednesday, May 14

American Association for the Study of Goiter. Hotel Statler, Boston.

*9–10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*12 m. Clinicopathological conference. Children's Hospital.

*8:15 p.m. Francis Amory Awards. American Academy of Arts and Sciences, 28 Newbury Street, Boston.

Thursday, May 15

*9–10 a.m. Some of the Effects of Flying on the Cardiovascular System. Dr. Ashton Graybiel. Joseph H. Pratt Diagnostic Hospital.

*8:15 p.m. Diagnosis and Management of Large Bowel Lesions. Dr. Richard Cattell. United States Naval Hospital, Chelsea.

Friday, May 16

*9–10 a.m. Early Diagnosis of Carcinoma of the Stomach. Dr. B. B. Crohn. Joseph H. Pratt Diagnostic Hospital.

*12:30 p.m. Sprue versus Ileojejunitis. Dr. Burrill B. Crohn. Boston Dispensary.

Saturday, May 17

*9–10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*Open to the medical profession.

May 11 — Boston Doctors' Symphony Orchestra. Second annual concert. Page 790, issue of May 1.

May 12–14 — American Association for the Study of Goiter. Page 753, issue of April 24.

May 13–16 — National Gastroenterological Association. Page 791, issue of May 1.

May 14 — New England Obstetrical and Gynecological Society. Page 752, issue of April 24.

May 15 — Trudeau Society of Boston. Page 834.

May 20 — South End Medical Club. Page 834.

May 21 — Massachusetts Medico-Legal Society. Page 785, issue of May 1.

May 21, 22 — Massachusetts Medical Society, Boston. Page 781, issue of May 1.

May 28–June 2 — American Board of Obstetrics and Gynecology. Page 262, issue of February 6.

May 29–31 — Medical Library Association. Page 671, issue of April 10.

May 30, 31 — American Heart Association. Hotel Statler, Cleveland.

May 30–June 2 — American College of Chest Physicians. Hotel Statler, Cleveland.

June 2 — American Medical Golfing Association. Page 785, issue of May 1.

June 2–6 — American Medical Association. Cleveland.

June 2–6 — Woman's Auxiliary, American Medical Association. Hotel Carter, Cleveland.

June 4 — Harvard Medical Alumni Association. Page 790, issue of May 1.

June 22–24 — Maine Medical Association. Marshall House, York Harbor, Maine.

October 13–24 — 1941 Graduate Fortnight of the New York Academy of Medicine. Page 834.

October 14–17 — American Public Health Association. Page 579, issue of March 27.

District Medical Societies

ESSEX SOUTH

May 14 — Relation of the Doctor to the Law. Mr. Leland Powers. New Ocean House, Swampscott.

FRANKLIN

May 13 — This meeting will be held at 11 a.m. at the Franklin County Hospital, Greenfield.

MIDDLESEX SOUTH

May 14 — Page 752, issue of April 24.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Chest X-Ray Interpretation, with Special Reference to Tuberculosis. By J. Burns Amberson, Jr., M.D. 8°, paper, 48 pp., with 30 illustrations. New York: National Tuberculosis Association, 1941.

Popular Home Remedies and Superstitions of the Pennsylvania Germans. By A. Monroe Aurand, Jr. Foreword by Logan Clendening, M.D. 8°, paper, 32 pp. Harrisburg, Pennsylvania: The Aurand Press, 1941. 25c.

Emergency Surgery. By Hamilton Bailey, F.R.C.S. (Eng.), surgeon, Royal Northern Hospital, London, surgeon and urologist, Essex County Council, surgeon, Italian Hospital, consulting surgeon, Clacton Hospital and the County Hospital, Chatham, and external examiner in surgery, University of Bristol. Fourth edition. 8°, cloth, 944 pp., with 930 illustrations. Baltimore: Williams and Wilkins Company, 1940. $15.00.

The Therapeutics of Internal Diseases. Vol. III. Supervising editor: George Blumer, M.D., David P. Smith Clinical Professor of Medicine, Yale University School of Medicine, and consulting physician to the New Haven Hospital. Associate editor: Albert J. Sullivan, M.D., adjunct clinical professor of medicine, George Washington and Georgetown medical schools, and chief medical officer, Gallinger Municipal Hospital, Washington, D. C. 8°, cloth, 738 pp., with 1 chart, 39 illustrations and 2 tables. New York: D. Appleton-Century Company, Incorporated, 1941. Sold only as a set. $40.00.

Schizophrenia in Childhood. By Charles Bradley, M.D., medical director, Emma Pendleton Bradley Home, East Providence, Rhode Island. 8°, cloth, 152 pp. New York: The Macmillan Company, 1941. $2.50.

Modern Drugs in General Practice. By Ethel Browning, M.D. 8°, cloth, 236 pp. Baltimore: Williams and Wilkins Company, 1940. $3.00.

Malignant Disease and Its Treatment by Radium. By Stanford Cade, F.R.C.S., surgeon, Westminster Hospital, Mount Vernon Hospital and the Radium Institute, lecturer in surgery, Westminster Hospital Medical School, and associate examiner in surgery, University of London. 4°, cloth, 1280 pp., with 623 illustrations, many in color. Baltimore: Williams and Wilkins Company, 1940. $18.00.

Biological Symposia. Vol. I. *The Cell Theory: Mating types and their interactions in the ciliate infusoria; chromosome structure.* Edited by Jaques Cattell. With a foreword by Albert F. Blakeslee, Ph.D. 4°, cloth, 238 pp., with 39 illustrations and 19 tables. Lancaster, Pennsylvania: The Jaques Cattell Press, 1940. $2.50.

Biological Symposia. Vol II. *Speciation: Defense mechanisms in plants and animals; biological basis of social problems; regeneration.* Edited by Jaques Cattell, with a foreword by George A. Baitsell, Ph.D. 8°, cloth, 270 pp., with 13 illustrations and 1 table. Lancaster, Pennsylvania: The Jaques Cattell Press, 1941. $2.50.

BOOK REVIEWS

The Management of Obstetric Difficulties. By Paul Titus, M.D. Second edition. 8°, cloth, 968 pp., with 368 illustrations and 5 color plates. St. Louis: The C. V. Mosby Company, 1940. $10.00.

The title *The Management of Obstetric Difficulties* is hardly broad enough to include all the valuable material presented in this volume. For instance, the first two chapters are devoted to the treatment of sterility, including a well-illustrated discussion of the treatment of absolute sterility in the male.

The section on the complications of pregnancy contains many valuable features, including a detailed discussion of the so-called "minor complications" and the treatment of various systemic diseases and conditions requiring surgery during pregnancy. The important subject of infections of the urinary tract is well covered.

The methods of diagnosis and treatment in cases of ante-partum hemorrhage are by no means standardized, and naturally not everyone will agree with the author's opinions. He does not mention the latest advances in soft-tissue roentgenography in the diagnosis of placenta previa; he favors cesarean section in cases of complete separation of the placenta, in spite of recent statistics that show a lower mortality following normal delivery.

Two chapters deal with the toxemias of early and late pregnancy, and this subject is particularly well covered by the author, who has devoted much study to it.

Complications of labor, obstetric operations and complications of the puerperium are considered in detail. The author is conservative with regard to the use of pituitary extract in the first stage of labor, to the point of withholding it, even in small doses, in patients who are suffering from uterine inertia. Emphasis is properly placed on strict asepsis in connection with all obstetric surgical procedures, and all the operations are described in minute detail.

Two chapters are devoted to the care of the newborn infant, and the last four chapters deal with the actual preparation for delivery and aftercare of the patient, including a discussion of the various types of obstetric anesthesia and analgesia, and concluding with a description of the technic of preparation and injection of dextrose solution and of blood transfusion. Here, again, the subjects, although interesting and useful, do not seem to belong in a book devoted to obstetric difficulties.

Because of its attention to detail, this book is particularly useful when an unusual complication is encountered; it is to be recommended for ready reference.

A Review of the Psychoneuroses at Stockbridge. By Gaylord P. Coon, M.D., and Alice F. Raymond, A.B. 8°, cloth, 299 pp., with 66 tables and 2 figures. Stockbridge, Massachusetts: Austen Riggs Foundation, Incorporated, 1940. $2.00.

From the standpoint of psychotherapeutics, this is an excellent book. It gives in detail and very cogently the technic used at Stockbridge and the results obtained. Whatever statistical evaluation is made of the results, however, is to a certain extent impaired by the fact that the patients are a highly selected group: first, financially, and secondly, by reason of their background of training and experience. In other words, the segment of psychoneurotics under consideration is probably far more accessible to the treatment described in this book than any other conceivable group of sufferers from neuroses.

One might easily criticize the classification of the types discussed in the first part of the book. When the seven groups are viewed objectively, it is found that practically every conceivable type of personality develops neurosis, since the classification goes all the way from the group of "overly ambitious, conscientious, dynamic, energetic persons" in Group A to the "immature, dreamy, romantic persons" of Group E, and includes all the way-stations of personality in between. To attribute a neurosis to hard, driving work without enjoyment and then to find that people of opposite temperament develop exactly the same symptoms cancels the classification of causes or of pertinent factors that are probably nonrelevant.

The reviewer still believes that the cause of the neurosis is unknown. One can postulate, in the present state of knowledge, that emotional stress, maladjustment in life, trouble or trauma — physical or mental — precipitates symptoms. But the essential basis is still a matter for future research to uncover. Adding inconclusive factor to inconclusive factor, no matter how many times, does not bring conclusiveness. Nor does the comparison of results of the Stockbridge cases with those of other institutes seem very convincing. The Stockbridge sample includes only neurasthenia or anxiety states, whereas that of the New York Psychiatric Institute, for example, includes compulsion neuroses as well, probably patients extremely unfortunate in all the circumstances of life, and also those having severer neuroses, that is, those leading to commitment or at least care in a hospital for mental disease. This at once excludes the minor cases.

Despite these criticisms, the book is, on the whole, excellent. It is clear, frank and intelligent in its discussion of the neuroses. The concluding section, which deals with mental hygiene and maladaptation, is excellent and is recommended to the general practitioner as well as to the psychiatrist. The book does credit to the institute from which it emanates.

Landmarks and Surface Markings of the Human Body. By L. Bathe Rawling, M.B., B.Sch. (Cantab.), F.R.C.S. Eighth edition. 8°, cloth, 98 pp., with 36 illustrations. New York: Paul B. Hoeber, Incorporated, 1940. $3.00.

This little volume offers a handy reference to the surface topography of anatomic structures. Although such treatises are of special interest to surgeons, internists will be interested in the data on the viscera of the cranium, thorax and abdomen, particularly since they relate to physical diagnosis.

The terminology of this eighth edition is revised to conform to the standard B.N.A. nomenclature.

Synopsis of Materia Medica, Toxicology and Pharmacology: For students and practitioners of medicine. By Forrest Ramon Davison, B.A., M.Sc., Ph.D. 12°, cloth, 633 pp., with 45 illustrations. St. Louis: C. V. Mosby Company, 1940. $5.00.

This book is a well-organized epitome of the subjects mentioned in the title. The first portion is devoted to general principles, and is followed by a description of drugs acting on the various systems, the metals and, finally, the biologicals. Despite its apparent conciseness, a great deal of ground is covered. The small type militates against any sustained reading, and hence lessens its value as a text. For quick reference it should prove very useful.